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Postgraduate Medicine

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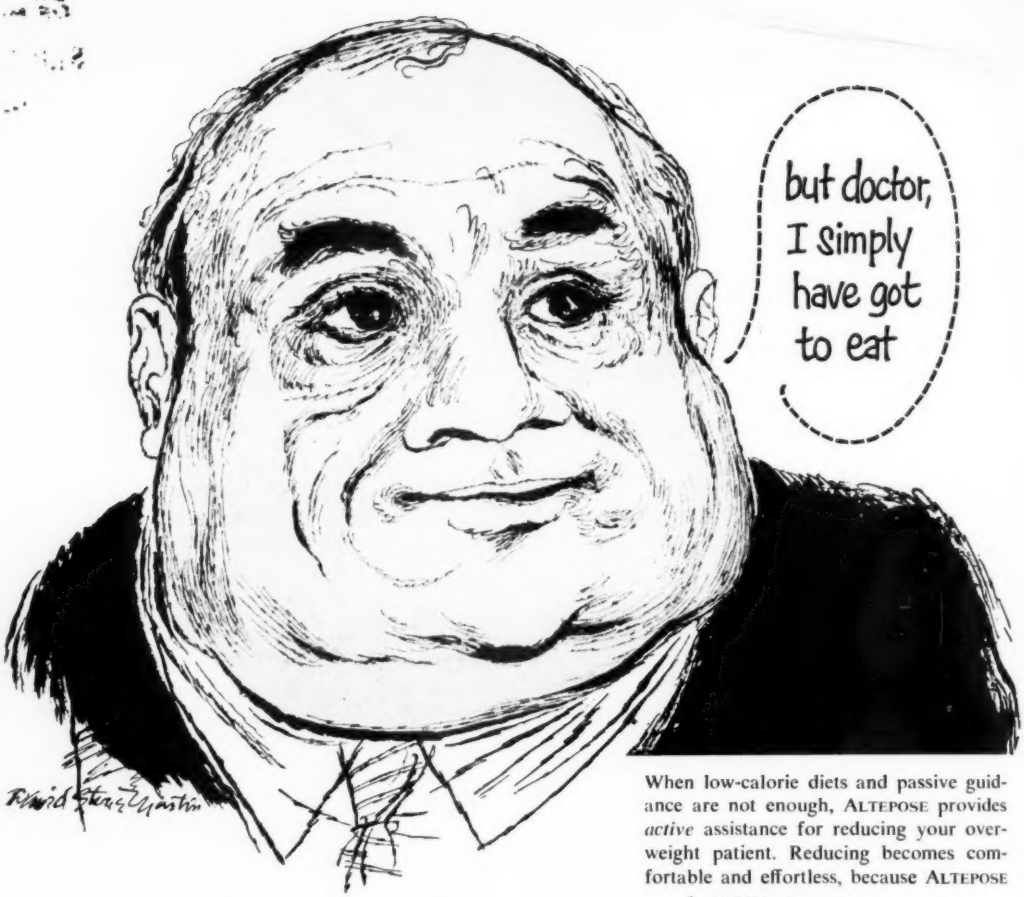

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References: 1. Jolliffe, N.: Reduce and *Stay* Reduced, Simon and Schuster, New York, 1952, p. 2. **2.** Tainter, M. L.: J. Nutrition 27:89, Jan. 1944. **3.** Kalb, S. W.: M. Soc. New Jersey 39:584, Nov. 1942.

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Your Questions answered

Readers may send questions from their own practice or other medical problems which will be answered by qualified consultants.

• HYDRARTHROSIS

Question: Has hydrocortisone been found useful in intermittent hydrarthrosis?

M.D.—Illinois

ANSWER: Hydrocortisone has been tried for intermittent hydrarthrosis in two ways. One schedule includes an injection of hydrocortisone into the affected knee at the onset of each attack. The attack so treated is lessened in its severity. However, subsequent attacks usually are not avoided. The other schedule is to give either hydrocortisone or cortisone by mouth at the onset of each attack. Each individual attack is also lessened during the treatment. However, subsequent attacks are not usually avoided. To give cortisone or hydrocortisone daily in a dose large enough to prevent recurrence requires so large a dose of these hormones that a hypercortisone state may develop, making the treatment impractical. So far as we can see, hydrocortisone or cortisone is not practical as long-term continuous treatment for intermittent hydrarthrosis but may be justified to help in the control of an individual attack of swelling.

• "JET" TECHNICS FOR ANESTHESIA

Question: Some years ago there was considerable mention in the lay press of high pressure sprays that would penetrate the skin almost painlessly and by which a hypodermic injection could be given. I wonder what has happened to this research? Has such a method proved impractical or is it available? I can see that dosages might be difficult, but if used only for NOVOCAIN® for local anesthesia in dermatology, it would be a boon. I would appreciate any information you can give.

M.D.—California

ANSWER: Research is still being carried on to develop a satisfactory instrument to administer various drugs and medication utilizing "jet" or high pressure technics. The R. Scherer Company of Detroit, Michigan, is still interested in this development, as is Becton, Dickinson and Company of Rutherford, New Jersey. Specific data concerning up-to-date releases on research should be requested of either of these sources.

CHARLES F. MC CUSKEY

• EFFECTS OF THYROID EXTRACT

Question: May I have your advice with reference to the use of thyroid extract? I have a patient, female, age 41, single, a homemaker, who was discharged from a mental hospital a year ago. Her physicians prescribed certain medications for her to use at home including multiple vitamins and Armour thyroid extract, 7½ gr. a day. She has been taking them since last fall. She has a B.M.R. taken every month or two and this has always been normal. There has been no weight loss, tachycardia or exophthalmos. Is there any danger in continuing with this dose of thyroid? Any suggestions you may wish to offer will be most gratefully received.

M.D.—Michigan

This inquiry was submitted to two consultants whose opinions follow:

ANSWER: Seven and one-half grains of Armour U.S.P. desiccated thyroid is an unusually large dose, and most people do not tolerate this without developing symptoms of hyperthyroidism. Up to 3 gr. daily of desiccated thyroid does not produce any significant changes in metabolism in a normal person. The thyroid merely stops functioning and the patient utilizes the exogenous thyroid instead of the product of his own gland.

(Continued on page A-30)

Every patient with essential hypertension is a potential candidate for Raudixin therapy

Because of its safety and the stability of its hypotensive effect, Raudixin can be confidently prescribed for all patients with essential hypertension. It is especially recommended for the large, indeterminate group whose symptoms are not severe enough to warrant the use of other hypotensive agents. Critical adjustment of dosage is unnecessary.

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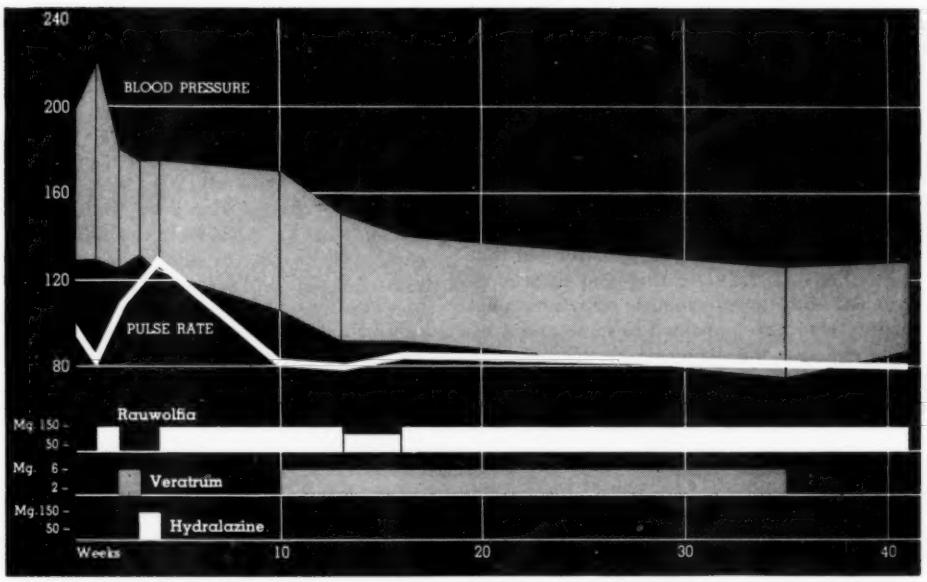

This patient's blood pressure was lowered about the same amount by rauwolfia, veratrum or hydralazine. Hydralazine, however, caused undesirable reactions and increased the pulse rate. Veratrum augmented the effect of rauwolfia, and the effect was maintained even when veratrum was discontinued some months later. – After R. W. Wilkins, Ann. Int. Med. 37: 1144, 1952.

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but above 3 gr. a day increase of metabolism and mild symptoms of toxicity usually can be expected. The patient either has compensated in some way for the increased thyroid or is not absorbing it well.

I do not believe there is any particular danger in continuing this dosage if the patient appears to be quite normal, but I would anticipate that reduction of the dose to 3 gr. daily would not be followed by any recurrence of whatever symptoms were being treated by the desiccated thyroid.

GEORGE CRILE, JR.

ANSWER: It is remarkable how large a dose of thyroid extract can be taken by people with euthyroidism or even by people with mild hypothyroidism. I would expect that the patient you mentioned falls in this category. In view of this and of the lack of evidence of a specific metabolic effect of the thyroid in this patient the probabilities are that she could continue without adverse effects. However, its value is certainly to be questioned. Thyroid extract is the *sine qua non* in the treatment of myxedema. The emotional and intellectual impairments seen in myxedematous patients respond well to thyroid, although their tolerance is so limited that only fractions of the dose that you mentioned are usable. Mild hypothyroidism with emotional instability may also be helped to some extent by thyroid although the diagnosis in evaluation of such cases is most difficult and unsatisfactory.

Other than these two specific examples, the use of thyroid in mental illness has not been met with great success. I would therefore question whether this woman has been helped by thyroid extract and would suggest probably that it is your continued help and interest that have been most valuable.

FRANKLIN G. EBAUGH

• SINUSITIS

Question: For about 10 years I have been treating adult patients with sinusitis in the following manner: Cotton swabs dipped in a solution of CLOPANE® (Lilly) and containing 2 per cent cocaine and 100,000 units of penicillin (refrigerated) are applied to the nares, one above and one below the middle turbinate. The swabs are left in place for one-half to one hour. I have interviewed patients carefully, and they state there is no "kick" or exhilaration as a result of the treatment. Am I justified in continuing this method?

M.D.—Minnesota

ANSWER: There is no particular objection to the use of Clopane applied locally within the nose, as far as I know. The application of penicillin locally in the nose or on the skin has been abandoned for the most part by rhinologists and by dermatologists because of the severe local reactions which can occur. The only effect such penicillin could have would be to kill organisms which come into contact with it. Penicillin applied in the middle meatus would certainly not do anything to organisms within the sinuses. The only way one can treat these organisms with penicillin is to introduce the penicillin through the blood stream (except by irrigation with penicillin solutions, largely abandoned at present).

Two per cent cocaine does produce a "kick," despite what the patients have said. This can be verified by any doctor who cares to try the treatment himself or have someone else try it for him. The use of a habit-forming drug repeatedly over a long period of time by topical application is certainly not justified. It does not do anything to the sinuses except possibly open the ostia and drain them. Whether it is wrong or not depends entirely on how frequently it is applied in a particular case. Obviously if the patient has 2 or 3 applications and does not return for treatment for many months or even for a year or two, there is nothing wrong with the treatment and, as a matter of fact, it is probably well justified. On the other hand, if the patient does not actually have sinusitis but simply has headaches on a vascular basis or some other complaint, and returns frequently to have the treatment, of course this is wrong. The use of 2 per cent cocaine in the nose is compatible with ciliary activity and does not disturb the nasal physiology unduly.

ROBERT E. PRIEST

Treatment of Facial Injuries and Deformities

CLAIRE L. STRAITH AND RICHARD E. STRAITH*

Straith Clinic, Detroit, Michigan

Which facial deformities can be improved and when operation should be done are of vital concern to patients so afflicted. This article deals with the correction of numerous deformities so as to increase considerably the mental well-being and economic independence of these persons.

CLAIRE L. STRAITH

RICHARD E. STRAITH

THIS year one million persons in this country will be injured in auto accidents alone, and 40,000 probably will be killed. Of the million injured, it is probable that thousands will have their future prospects for financial success, marriage, etc., ruined entirely or seriously jeopardized by hasty and careless treatment of their facial injuries. Hospital reputations can be ruined when these facial wounds are poorly cleansed, or closed with skin clips or heavy materials, resulting in conspicuous pigmented or suture-marked scars (Figure 1). Such wounds are a poor "ad" for any hospital and may ruin a victim's life.

Interns or emergency room staffs should not be turned loose without instructions as to the careful treatment of facial wounds. They should be instructed as to the careful cleansing of all facial wounds, irrigations to remove dirt and foreign matter, and removal of brush burns, cinder marks, etc., by scrubbing with hand brushes. These things must be done at once or the dirt becomes imbedded and pigmented scars result.

Surgical instruments should be furnished suitable for use in careful trimming of the jagged wound edges—hooks instead of forceps for the atraumatic handling of tissues, and fine needles for meticulous subcuticular suturing so that as fine a scar as possible can be produced (Figure 2). After careful cleansing of the wound and trimming the irregular edges, we place fine white NYLON® sutures through the dermis, tied with the knot most dependent. This should cause slight eversion of the wound. Fine nylon subcuticular sutures are then inserted, care being taken that they are the same depth on each side of the wound. Any irregular areas are closed with very fine silk or nylon interrupted sutures and in this way we believe facial scarring is reduced to the minimum (Figure 3).

*Straith Clinic for Plastic and Reconstructive Surgery, Detroit, Michigan.

Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

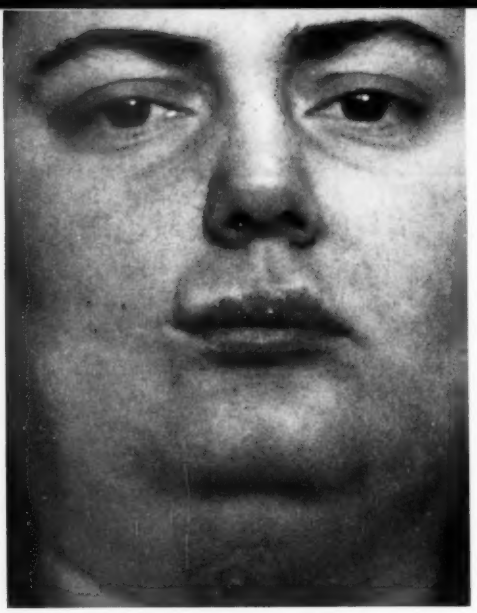

FIGURE 1. In wounds involving the mouth or nose it is important to approximate the borders accurately with figure of 8 nylon sutures tied inside the nose or mouth to relieve tension. The surface portion of the wound is then closed with fine buried white nylon with the knot at the bottom of the wound, and a 4-0 or 5-0 nylon subcuticular suture as described in Figure 3. The vermilion borders should be approximated very accurately. This patient shows results of such primary closure of the wounds.

Facial bone fractures should, of course, be looked for and treated at the same time, if possible, but this is a subject in itself and cannot be included here.

Disfiguring old facial scars often can be greatly improved by careful excision and closure with subcuticular sutures. Depressed scars can be elevated by interdigitating fat flaps beneath the skin to prevent adhesions and depressions. Large depressions can be built up by cartilage or fat grafts.

In spite of all efforts to elevate and maintain good position of crushed nasal bones, a marked depression often results. By means of a profilometer, the amount of depression below normal can be measured (Figure 4). A

FIGURE 2 *(above)*. When the skin edges are greatly traumatized, it may be impossible to obtain good results at time of injury. These scars were excised in two operations beginning three months after the original injury, and the wounds closed as described in Figure 3.

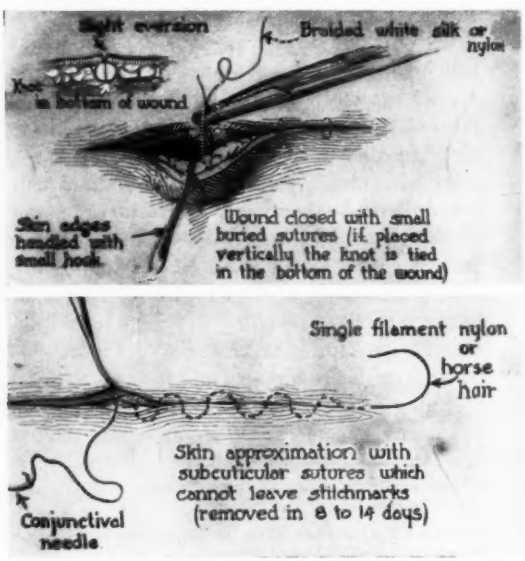
Slight eversion
Braided white silk or nylon
Knot in bottom of wound
Skin edges handled with small hook
Wound closed with small buried sutures (if placed vertically the knot is tied in the bottom of the wound)
Single filament nylon or horse hair
Skin approximation with subcuticular sutures which cannot leave stitchmarks (removed in 8 to 14 days)
Conjunctival needle

FIGURE 5. Depressed malar fractures should be diagnosed and elevated early, as in this case. Late attempts to raise them are usually futile. In this event, preserved cartilage grafts are used to restore normal facial contour.

preserved cartilage or bone transplant is then carved to fit the defect and inserted through an incision in the columella of the nasal tip.

Occasionally, depressed malar bone fractures, which usually can be elevated by the intraoral route, are left or unrecognized, resulting in a decided lowering of the orbital floor and eyeball, and diplopia. This can be corrected by inserting a piece of preserved cartilage in the floor of the orbit to raise the eyeball to the proper level (Figure 5).

"Save the pieces" would be a good motto for all who ride in automobiles and therefore are potential accident victims. Severed ears, for instance, should be preserved, for the natural ear cartilage forms the best matrix

FIGURE 3 *(left)*. It is essential that the buried white nylon sutures bring the skin edges almost together before the subcuticular suture is used. Excess subcutaneous fat is debrided before suturing.

FIGURE 4 *(right)*. The profilometer is used to measure the amount of cartilage needed to build the nose up to normal. Columellar incision made for insertion of the cartilage is usually almost invisible within a few months.

FIGURE 6. "Save the pieces" should be the motto of all ambulance drivers and accident victims. The skin of this severed ear was removed and the cartilage was buried under the skin of the scalp three hours after the injury.

FIGURE 7. Two months later the skin and cartilage were elevated and a skin graft was placed behind the cartilage graft and against the scalp. The final result is much better than would have been obtained if preserved cartilage or some other form of support had been used.

FIGURE 8. Avulsed wounds such as this dog bite can be repaired during the first 24 hours following injury by full-thickness grafts taken from behind the ear. These grafts match the facial skin very well and usually take 100 per cent.

for reconstruction of the new ear (Figure 6). The skin can be denuded from the severed ear and the cartilage carefully preserved. Through the ear wound, the skin over the mastoid process can be carefully elevated and the ear cartilage slipped under the skin and the wound closed. After 60 days, when the cartilage has been grafted in place, an incision is made behind the grafted cartilage, the skin and cartilage elevated and a mold made of the cavity behind the buried cartilage. A thin skin graft is then wrapped around the mold and it is reinserted and the wound closed. After two weeks the mold is removed and the skin is found grafted to the back of the ear and the scalp (Figure 7). Further improvements can be made by grafting a pencil-sized roll of skin around the edge of the new ear.

In some cases, the grafting of the recovered piece may fail, as in a case where the tip of the nose had been severed. The nose tip was

found on the cowl of the car three hours afterward and brought to the hospital. It was carefully sutured in place but in spite of all efforts, the graft died, probably due to the three hour lapse of time following the accident. The nose was then reconstructed by using a forehead pedicle and subsequently returning the remainder of the flap to the forehead where the hairdress covers the defect.

Both children and adults frequently lose portions of the facial skin, especially the nose, due to dog bites. If these areas are kept clean, skin grafts from behind the ear can be used for covering, even 24 hours after such an injury, and much time saved in the recovery period (Figure 8). These full-thickness grafts should be cut to the pattern of the defect, sutured in place with fine silk and the sutures tied over a pad of gauze to produce pressure.

Defects of the nasal tip can be repaired later by several means, one of the most useful being a nasolabial flap which leaves only a very inconspicuous secondary scar in a natural fold of the face (Figures 9 and 10).

Congenital deformities are always distressing to all concerned. For this reason, we feel that harelips, for instance, should be repaired as soon after birth as feasible—usually we do this on the fifth to seventh day (Figure 11). These babies are given a small amount of paregoric or sedative per rectum and a local anesthetic is injected around the infraorbital nerves and base of the nose. Young children retain their pharyngeal reflexes and there is less danger of aspiration than when general anesthesia is employed. The head is strapped in a "doughnut" to prevent movement and operation can proceed with little difficulty.

Afterward they are fed by gavage or an indwelling plastic tube and the sutures are kept moist with penicillin ointment. We feel that it is very important to have all the tension re-

FIGURE 9 *(left)*. Less extensive skin losses about the nasal tip can be repaired by swinging a nasolabial flap into the defect. At the first operation parallel incisions are made down the nasolabial fold and the flap is undermined. The wounds are closed with subcuticular sutures.

FIGURE 10 *(right)*. At the second operation the flap is cut off at the inferior end, wrapped around into the nostril to form an inside lining and an outside covering, and sutured into place. At the next operation the flap is severed and the upper border of the new ala is then sutured to the nasal skin. Three weeks later the final trimming and thinning of the flap are done.

lieved by placing figure of 8 sutures *inside the lip* to prevent suture marking. The surface is then closed with 6 or 8-0 black silk or subcuticular 5-0 nylon which leaves even less scarring. There are many adults with harelip scars that are very conspicuous. These persons often are very self conscious and lead secluded lives where possible rather than suffer the embarrassment of constant stares. Modern plastic procedures can be carried out on these lips and the deformities greatly improved. The lives of these persons can thereby be made infinitely happier.

Many children also have cleft palates, which we have found by experience are best left alone until the child is just ready to talk. Two years seems about the ideal age to attempt these closures, although operation can be done at any age, one patient in our clinic being 67 years old!

Other facial deformities, such as moles of all sizes, present problems in correction. Small moles usually can be excised in one or more stages. Some larger moles require large skin grafts which subsequently can be reduced in size by multiple excisions. Other large and irregular moles require a combination of skin excisions, pedicle transfers, eyebrow grafts, etc., before acceptable results are obtained.

Ear deformities are very common in children and very conspicuous especially in boys. Congenitally small or missing ears usually require a series of about six operations, covering a period of 9 to 12 months for their reconstruction. The body of the ear is usually constructed over cartilage grafts buried under nearby skin and, in boys, the roll around the edge of the ear is brought up in two stages, as a tube pedicle from the chest. In girls, however, we hesitate to scar the neck or chest and the tube must come from elsewhere, usually the inside of the upper arm.

"Lop ears" are very distressing to small boys, and the constant ridicule from playmates who call them "mule ears," "elephant ears," "jug handle ears," etc., makes them antisocial. Girls usually can hide the ears with the hairdress but now, with the "upsweep" hairdress in fashion, they frequently seek correction (Figure 12).

Under local or general anesthesia, an ellipse of skin is removed from behind the ears and a smaller mass of cartilage is removed just below the anthelix, and the ears are sutured back with subcuticular sutures.

It seems better to correct all deformities in children wherever possible before school age and thereby spare them these embarrassing incidents. In writing about a child who had developed into a criminal as the result of ridicule, one author remarked, "Thus do the cruelties of youths create rogues."

One doctor told us that his boy, who was becoming almost unmanageable due to ridi-

FIGURE 11 *(left)*. Harelips should be closed as early as possible—usually by the end of the first week of life. If done at this time, the pressure of the united lip usually causes the cleft in the alveolar ridge to close by itself. If lip closure is delayed even a month or so, the cleft in the alveolar ridge, due to ossification, is much more difficult to close. At a later date the palate repair is much more difficult if the alveolar ridge is not closed.

FIGURE 12 *(right)*. Lop ears should be corrected as soon as the patient's sensitivity to the deformity becomes manifest. An ellipse of skin and cartilage is removed from behind the ear where the fold of the anthelix should be. The wounds are then closed with subcuticular sutures.

FIGURE 13 *(far right)*. Slight deformities often cause greatly exaggerated psychologic consequences. Correction at an early age should be advised where a marked sensitivity to any deformity exists.

cule about his ears, had changed his disposition entirely following the operation and now was a normal, well liked and well balanced child. We cannot emphasize too strongly the psychologic benefit that follows such operations on these deformed children.

One of the most distressing conditions that results in lifelong disfigurement is the acne of adolescence. Serious acne infections are difficult to combat and while present are extremely embarrassing to the victims. The resultant pits from acne infections, smallpox, etc., and also powder burns, can now be greatly improved by one or more sanding treatments, or occasionally by skin debriding with a dermatome. Under general anesthesia, the entire areas are thoroughly sanded with coarse sandpaper and the curves and folds treated with mechanical abrasion using bristle disks or small stones. The face is then covered with VASELINE® gauze, dry gauze and stockinet and left for 10 days, the sanded area being treated like a donor site after skin graft removal. One treatment will often suffice but several may be needed in deeply pitted faces. The results, however, are most gratifying to this group of self-conscious patients.

Nasal deformity probably is the most common condition the plastic surgeon is called on to treat (Figure 13). In fact, probably only a small percentage of the people seen on the street have noses that are ideal according to our usual conception. It is quite well agreed that the proper esthetic angles for a nose are as follows: The profile angle—or angle that the nose stands out from the face—should be about 30 degrees. The tip angle in a man should be about 90 degrees or a little more, but in a woman it should be 20 to 25 degrees above a right angle, depending on the chin line, age, etc. As we get older, the tip of the nose drops, and therefore simply shortening the tip of the nose will take years off the facial appearance.

These angles can be measured by the authors' profilometer and then, by giving the patient a second mirror and applying the profilometer at normal, the patient can see for himself or herself what changes we hope to accomplish by reducing the nose to normal, using the profilometer as a guide.

The operation can be done best under local anesthesia and can be done at any age after 15 years. We suggest to mothers that if the children are developing a complex about their noses, they should be operated on at 15 to 17 years of age so they can go through high school, college and a matrimonial period unhampered by a complex and improved in appearance.

All incisions are made within the nose. After elevating the skin from the nasal bones, the profilometer, set at normal, is applied to the nose. Using this mark as a guide, the

FIGURE 14. Business women of advancing years often find it difficult to obtain employment due to their age and appearance. Many years of profitable employment can be added to the life span of these individuals. Excess facial skin was removed from this patient by an incision running from the temple down in front of the ear, around behind and up over the mastoid process. The skin of the entire face was then advanced posteriorly and upward until approximately 1 inch of excess skin was removed from both sides. Wounds in the visible areas were closed with subcuticular sutures.

hump is removed down to a 30 degree angle. The nose is shortened, narrowed and remolded to fit the patient's face more perfectly. Many nasal deformities are due to old fractures and therefore septal deviations are present and require submucous resections which are usually done at the same time.

Advancing years may add deformities to the face. The gradual dropping of the nasal tip, the relaxation of the eyelid skin into superfluous folds in both upper and lower lids and, in fact, the relaxing of the whole facial and neck skin may cause a premature aging appearance that works an economic handicap to such victims.

The following warning was given by Clark Tibbits of the Federal Security Agency, Washington, D.C., to 200 persons attending a geriatrics conference: "It is doubtful if we Americans can maintain leadership in world economy unless we learn to use the wisdom, skills and productive capacity of our older citizens. Older people want to be assigned tasks or roles that enable them to feel they are contributing and that they are important. They want to be producers, not merely consumers. They want to be independent and self sufficient."

If, by carefully planned surgical procedures, these telltale aging signs can be eliminated, many years of profitable employment can be added to the life span of these individuals. Such an operation not only is an economic uplift, but also is a great morale builder. These patients have a new zest for life and their jobs (Figure 14).

In these patients with prematurely relaxed skin, an incision can be made within the temple hairline down around the ear and back into the scalp over the mastoid process. From this incision, the skin of the face and neck can be undermined, advanced upward and the excess skin resected, leaving the scars mostly within the hairline and therefore almost unnoticeable. Such an operation that may subtract years of age from the facial appearance and add years of profitable employment would seem to be as justifiable as repair of hernia or any other incapacitating condition.

One such patient, a 61 year old woman who underwent operation two years ago, expressed the feeling of many when she said that she wanted this operation not for vanity, but as a necessity, to keep her job.

Summary

We feel that the application of plastic principles designed to minimize deformities should be a "must" in the care of accident cases. Congenital or acquired deformities in children should be corrected before school age if possible and deformities should not be treated as "acts of God" to be borne with equanimity but should be corrected as early as possible to prevent or eliminate inferiority complexes and add joy to the lives of these victims.

Since medical science is now keeping alive thousands of persons into advanced years, more attention should be given to surgical procedures designed to restore a semblance of their more youthful appearance. In this way more and more able-bodied men and women can keep their jobs and self respect and remain economically independent in spite of the present social reforms that would tend to make us all wards of the state before retirement was necessary.

Optimism in the Treatment of Gastrointestinal Carcinoma

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In order that patients with gastrointestinal carcinoma achieve a maximum survival rate, it is necessary to adopt a prudent attitude of optimism, not only toward those with early lesions but also those who appear to have advanced disease. Eight cases are reviewed in which the patients, following radical surgery, are enjoying long periods of survival, even though the initial clinical picture seemed hopeless.

H. M. BLEGEN

THE outlook for patients with gastrointestinal cancer is at times discouraging. Because of the silent nature of the growth and errors in early diagnosis, many of these unfortunate individuals present themselves with far advanced and often hopeless disease. Therefore it is not surprising that an attitude of pessimism often prevails, not only among patients but also among physicians.

The treatment of choice for early carcinoma of the gastrointestinal tract is radical surgery. But since the treatment has been well described as a philosophy rather than a technic, there is, in cases of advanced disease, an understandable difference of opinion concerning operability, resectability and palliation. The conservative surgeon, perhaps with some justification, occasionally performs a palliative colostomy, ileocolostomy or gastroenterostomy in patients with admittedly advanced, but still technically resectable, lesions. Similarly the sincere physician often feels that surgery for advanced cancer of the stomach is only a futile gesture. On the other hand, in reviewing the recent literature, one is impressed by the increasing attitude of radicalism that now prevails in many of our larger medical centers. This is due largely to improvements in preoperative and postoperative care which have made possible the performance of rather extensive operative procedures with reasonable mortality and morbidity rates. Brunschwig[1,2] has performed extensive resections on patients with lesions which would ordinarily be considered hopeless; McNeer[3] has attempted secondary resections for recurrent carcinoma, and Wangensteen[4] has advised second-look procedures in patients who at operation are found to have lymph node involvement. All these more aggressive efforts

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are being made in the hopes that we may not only increase the salvage rate but also offer these patients longer and more comfortable lives and at the same time determine more fully the maximum effectiveness of surgery.

Whipple,[5] in considering the problem of operability, warns that we should offer these individuals every chance of cure, but in so doing we should temper our enthusiasm by carefully considering the spread of disease, the chance of survival, relief of symptoms and, finally, the ability of the patient to adapt himself to the disturbed anatomic and physiologic arrangement.

A recent review of a personal series of 160 cases of gastrointestinal carcinoma revealed that from the history and physical findings alone it was often difficult to determine with any degree of accuracy the extent of the disease or the resectability of the lesion. In a group of 52 patients with carcinoma of the stomach, the resectability rate was essentially the same (65 to 70 per cent) in those patients with histories dating back two or more years as in those patients with histories of less than two months. Several patients with small early carcinomas of the sigmoid were found at operation to have extensive liver metastases. On the other hand several patients had been ill for many months with large, bulky growths of the rectum and cecum which at operation were readily resectable. Factors such as the duration of symptoms, size of the mass, degree of emaciation, dehydration and anemia were not always signs of hopelessness. These symptoms were often secondary to bleeding or obstruction and occasionally they were due to benign lesions which from clinical evidence alone appeared to be malignant.

For these reasons, in order to obtain the maximum survival rate it seems necessary, whenever possible, to explore by laparotomy all patients with gastrointestinal cancer, unless hopelessness can be proved absolutely, preferably by biopsy of distant metastases. All lesions which are technically resectable should be widely removed along with the regional lymphatic system and adjacent organs, when involved. Even when distant metastases are present, increasing evidence suggests that palliative resection of the growth will not only prolong the patient's life but also make him more comfortable. If resection is impossible every effort should be made to relieve obstruction by some sort of a palliative sidetracking procedure.

In this report, in an attempt to justify such an aggressive and optimistic approach to the problem of gastrointestinal cancer, I wish to review briefly the case records of 8 patients who were thought before operation to have advanced or hopeless cancer but who, after radical surgery, are either cured of their disease or enjoying long periods of survival. I am sure that all these patients would have died with an erroneous clinical diagnosis of hopeless cancer if definitive surgery had not been performed.

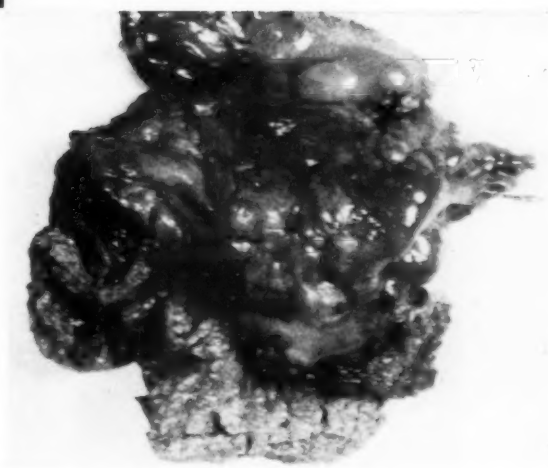
Large Carcinoma of Rectum

Case 1—A 43 year old woman with a large, bulky carcinoma of the upper rectum had been ill for over a year with increasing change in bowel habits, blood in the stools, rectal distress and abdominal cramps. Eleven months previously hemorrhoidectomy had been performed, although on rectal examination the carcinoma was within reach of the examining finger. The mass could also be felt by abdominal examination. Abdominal exploration revealed a large annular carcinoma in the upper rectum at the level of the peritoneal reflection. The growth had extended through the serosa of the bowel and was adherent to the lateral peritoneum. Numerous mesenteric nodes were involved. Radical combined abdominal-perineal resection was followed by an uneventful convalescence, and three and one-half years later this patient was in good health with no apparent recurrence of the carcinoma. (Figure 1.)

Comment—This case is reported because it emphasizes the fact that large, long-standing growths of the rectum are occasionally curable even when local extension or node involvement has occurred. Although lesions of this type are quite common, they are occasionally considered hopeless and treated by simple colostomy. This not only denies the patient his chance of cure but also leaves him with all

FIGURE 1 *(left)* (Case 1). Large carcinoma of the rectum with local extension and node involvement.

FIGURE 2 *(below)* (Case 2). Carcinoma of transverse colon with gastrocolic fistula. Block resection of the stomach (top), colon (center) and omentum (bottom).



the distress associated with an expanding rectal neoplasm. Unlike carcinoma of the stomach the outlook for patients with cancer of the rectum is fairly good; therefore, all these lesions should be removed whenever possible even though an adequate resection may require the removal of adjacent organs such as uterus, ovaries, small bowel or portions of the bladder.

Carcinoma of Colon with Gastrocolic Fistula

Case 2—A 45 year old woman had a large carcinoma of the splenic flexure of the colon with a gastrocolic fistula. She had been ill for one year with soreness in the left upper abdomen, abdominal cramps, occasional diarrhea, blood in the stool and weight loss of 16 pounds. A large, nodular mass was palpable in the left upper abdomen. Operation was performed in December 1948. The mass was removed by block resection of the left half of the transverse colon, two-thirds of the stomach and a portion of the abdominal wall. Intestinal continuity was restored by Hofmeister gastrojejunal anastomosis and end to end aseptic anastomosis of the colon. Pathologic examination of the specimen revealed a large adenocarcinoma (grade 2, type 3) of the transverse colon with a malignant gastrocolic fistula. Convalescence following surgery was uneventful; the patient gained 20 pounds in weight and three years and three months later was apparently well with no evidence of recurrence. (Figure 2.)

Comment—Gastrocolic fistula is a rather unusual condition which occasionally occurs in advanced carcinoma of the stomach or colon, but which is more often associated with a penetrating gastrojejunal ulcer following gastroenterostomy.[6] In the case just reported, the situation at operation seemed more or less hopeless, but because the growth was technically resectable it was removed as a palliative gesture. Since this patient has now survived more than three years, the chance of cure seems good, but should she develop a recurrence, evidence suggests that the radical surgery performed was of palliative value.

Polypoid Carcinoma of Cecum with Intussusception

Case 3—A 62 year old woman had been ill for five months with recurrent bouts of abdominal cramps, intermittent diarrhea, blood in the stool, vomiting, marked weight loss, anemia and cachexia. Examination of the abdomen revealed a large, hard, multinodular mass extending across the upper abdomen. Because of the size of the mass, marked emaciation, dehydration and anemia, this patient had been advised that she had an advanced, inoperable cancer of the bowel.

Operation performed in March 1949 showed a polypoid tumor of the cecum forming an intussusception which extended almost to the splenic flexure of the colon. The primary tumor was pedunculated, well localized and easily removed by right hemicolectomy and end to side ileotransverse colostomy. Pathologic examination revealed a grade 2 polypoid adenocarcinoma with no evidence of extension. Following surgery the patient made a smooth convalescence and is now apparently cured. (Figure 3.)

FIGURE 3 (Case 3). Large malignant polyp of right colon forming massive intussusception.

Comment—This patient had an early, very operable lesion of the right colon, which because of intussusception was thought to be a hopelessly advanced carcinoma of the transverse colon. The symptoms in this case were all secondary due to the intussusception. Abdominal exploration was attempted after extensive preoperative preparation even though the chances of cure seemed remote. The growth was easily curable.

Chronic Fibrosing Pancreatitis

Case 4—A 42 year old man had a large tumor of the head of the pancreas with increasing upper abdominal distress and low grade jaundice. Several months previously an abdominal operation had been performed and the gallbladder drained. At that time his wife was informed that he had a malignant tumor of the head of the pancreas and that the outlook for survival was poor. Exploratory laparotomy was again performed because of recurrent jaundice. He was found to have a large, hard tumor mass in the head of the pancreas with obstruction of the common duct. The mass was thought to be malignant even though the diagnosis could not be confirmed by biopsy. Therefore, a Whipple operation was performed. Pathologic examination of the specimen revealed a benign fibrosing pancreatitis with no evidence of malignancy. The postoperative convalescence was satisfactory and four years later the patient had a low grade diabetes but was doing fairly well if he avoided alcohol. (Figures 4 and 5.)

Comment—Localized benign fibrosing pancreatitis is a condition which causes common duct obstruction more often than is generally realized. Many of these lesions in the past were diagnosed as carcinoma of the head of the pancreas. At operation it is often difficult to make a differential diagnosis even when biopsies are made. When the diagnosis of

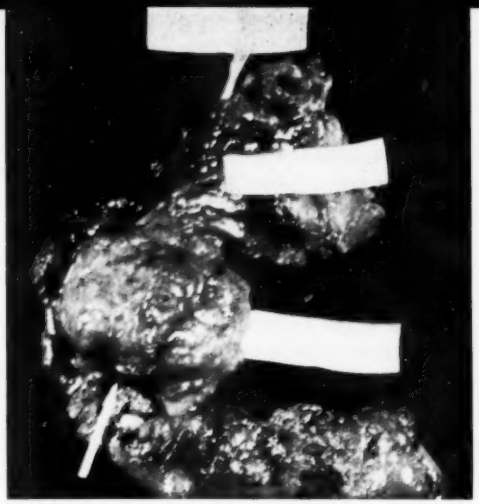


FIGURE 4 (Case 4). Tumor of head of pancreas with common duct obstruction. Benign fibrosing pancreatitis.

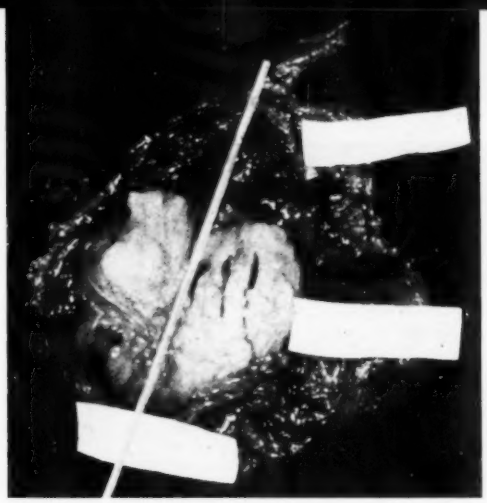


FIGURE 5 (Case 4). Localized benign fibrosing pancreatitis with common duct obstruction—thought to be carcinoma.

malignancy is definitely established, a Whipple operation should be performed if the patient's general condition permits. Cattell,[7] however, in a recent review has shown that as yet no case of pancreatic malignancy has been cured by this procedure; therefore, if there is any question as to the diagnosis it is perhaps best to perform an initial side-tracking procedure followed at a later date by a second abdominal exploration.

Large Benign Gastric Ulcer

Case 5—A 64 year old white man had a tremendous gastric ulcer involving over 50 per cent of the stomach with penetration into the body of the pancreas. Because of the size of the abdominal mass, the tremendous defect on gastric fluoroscopy and a severe cachexia, he was thought clinically to have a hopeless carcinoma.

Exploratory operation was performed and even though numerous lymph nodes were palpable the growth was removed by total gastrectomy and partial pancreatectomy. Subsequent pathologic examination of the specimen revealed a large benign ulcer with no evidence of malignant change. Following surgery this patient had an uneventful convalescence. He gained 30 pounds in weight, and four and one-half years later, he was apparently cured of his disease. (Figures 6 and 7.)

Case 6—An 82 year old man had a large diaphragmatic hernia with a large ulcerating

FIGURE 6 *(above)* (Case 5). Large benign gastric ulcer, thought to be hopeless gastric carcinoma.

FIGURE 7 *(below)* (Case 5). Large benign gastric ulcer with central penetration into pancreas.

FIGURE 8 (Case 6). Diaphragmatic hernia of stomach. Large gastric ulcer in cardia.

lesion in the cardia causing obstruction at the cardioesophageal junction. X-ray and esophagoscopy suggested carcinoma although the diagnosis could not be confirmed by biopsy. Previously he had been informed that he had an advanced carcinoma of the lower esophagus but that surgery was impossible because of his age. He was treated by repeated esophageal dilations, but eventually operation was necessary because of complete esophageal obstruction. Total gastrectomy and Graham esophagojejunostomy were performed. Pathologic examination of the specimen revealed a large benign ulcer 8 or 9 cm. in diameter in the cardiac end of the stomach. There was no evidence of malignancy. The patient made a satisfactory convalescence. He gained 20 pounds in weight and one and a half years later was in good health and was very enthusiastic about the improvement in his general condition. (Figure 8.)

Comment—Both these patients had large gastric ulcers which, following clinical examination, were thought to be advanced carcinoma. In case 5 exploration and resection were done reluctantly because the internist, radiologist, pathologist and I all felt that the condition was hopeless. The benign nature of the ulcer was not fully appreciated until the microscopic sections were made.

In case 6 the patient was thought to have a carcinoma of the cardiac end of the stomach, but he had been denied surgery because of his age. I am sure that both these patients would have died with an erroneous diagnosis of gastric carcinoma if surgery had not been performed.

Carcinoma in Stomach with Enlarged Lymph Nodes

Case 7—A 53 year old man had a prepyloric carcinoma of the stomach associated with enlarged lymph nodes along the greater and lesser curvatures. He had been ill for eight months and complained of vague indigestion, loss of appetite and weight loss. At operation the growth was found to be readily resectable, but because of the node enlargement, prognosis seemed poor. A conservative partial gastrectomy was performed to remove the nodes and the omentum. Pathologic examination of the specimen revealed a well localized, ulcerating prepyloric carcinoma 8 cm. in diameter. Examination of the lymph nodes showed evidence of lymphadenitis but no evidence of metastatic carcinoma. The patient made a smooth recovery, and seven years later was in good health with no evidence of recurrence. (Figure 9.)

Comment—This case is of interest because it illustrates first that patients with carcinoma of the stomach can occasionally be cured and second that enlarged regional lymph nodes are not always a sign of advanced carcinoma. Occasionally node enlargement may be due to other disease or to an associated inflammatory reaction.

The outlook for patients with carcinoma of the stomach is at times discouraging, but certainly not hopeless. The over-all five year survival rate is probably not over 10 per cent, and in patients without node involvement seldom above 30 per cent.[4] This discouraging survival picture is due in part to difficulties

involved in early diagnosis and also to the inadequacy of partial gastrectomy as generally performed. Lahey's[8] opinion was that because of the silent nature of the tumor and the anatomic arrangement of the gastrointestinal tract, no great improvement in diagnosis can be expected until a simple test is developed which will enable us to detect these lesions in their early, asymptomatic stage. For the present, therefore, our only hope of improving the survival rate lies in an increasing effort at early diagnosis and a greater use of radical subtotal or total gastrectomy,[9] accompanied by meticulous gland dissection, especially in those patients with early lesions.

Carcinoma of Small Bowel with Brain Metastases

Case 8—A 55 year old man when first seen had all the signs and symptoms of brain tumor.[10] He was referred to a neurosurgeon (Dr. Paul Flothow) who, in April 1944, removed an encapsulated tumor from the left frontal lobe of the brain. Pathologic examination of the specimen revealed a metastatic adenocarcinoma. Subsequent x-ray studies failed to reveal the primary lesion. Finally, three months after the brain operation, abdominal exploration was performed because of increasing intermittent abdominal cramps. Exploration showed a polypoid carcinoma of the upper jejunum approximately 1 inch in diameter with intussusception. Three smaller benign polyps were present a short distance from the primary tumor. Wide jejunal resection and end to end anastomosis was followed by an uneventful convalescence. Pathologic examination of the jejunal lesion revealed a very malignant tumor similar in appearance to the brain tumor previously removed. Both slides were examined by five reputable pathologists, all of whom were of the opinion that this was a primary adenocarcinoma of the small bowel with a metastatic lesion of the brain. One felt that the lesion was a malignant melanoma but all gave a very grave

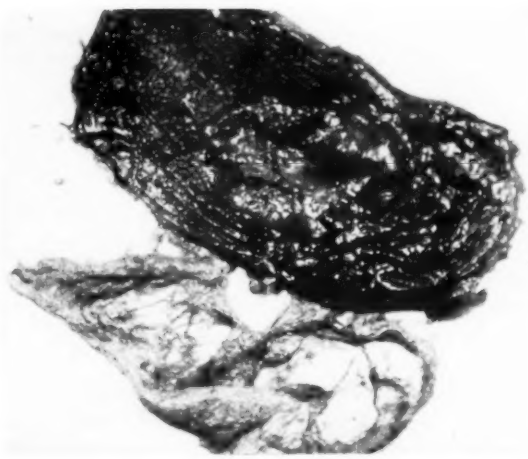


FIGURE 9 *(left)* (Case 7). Carcinoma of stomach; seven year survival.

FIGURE 10 *(above)* (Case 8). Carcinoma of the jejunum with brain metastasis; eight year survival.

prognosis and urged that careful autopsy be performed. The patient made a remarkable recovery. He returned to work and remained asymptomatic for two years. Then, in May 1946, he returned because of mild abdominal cramps of three weeks' duration similar to his initial distress. Reoperation in May 1946 revealed another intussuscepted polyp of the jejunum 6 inches distal to the previous anastomosis. Again the lesion was resected and the convalescence was uneventful. Pathologic examination of this second lesion showed a similar malignant jejunal adenocarcinoma. It was impossible to determine whether this was a recurrence or another primary lesion.

Since then the patient has had no further trouble. Eight years after his initial brain operation he weighed 210 pounds, was in good health and showed no evidence of recurrence. (Figure 10.)

Comment—Carcinoma of the jejunum is in itself a rather uncommon tumor. Eight years' survival in a patient with a metastatic brain lesion is almost unbelievable. This case is of interest because it warns us of the difficulties involved in making a prognosis and also supports the view that resection of solitary distant metastatic lesions is at times justifiable.

Summary and Conclusion

1. Eight cases are presented in which the clinical pictures suggested advanced or hopeless gastrointestinal carcinoma. Following surgery all of these patients either were cured of their disease or were enjoying long periods of survival. The difficulties involved in diagnosis and prognosis are emphasized by the fact that 3 of the patients had benign lesions, 2 had early, curable carcinomas, and 3 have been enjoying long periods of survival even though the disease was advanced. Since these cases were encountered in a rather limited personal experience, situations of this type are perhaps more common than is generally realized.

2. Evidence suggests that from the clinical picture alone, it is often difficult to determine the extent of the disease or the curability of the lesion. Factors such as duration of history, size of the mass or degree of emaciation are not always signs of hopelessness. Therefore, in order to obtain the maximum survival rate it is necessary to adopt a prudent attitude of optimism and offer these patients the benefits of radical surgery even though the chance of cure may seem remote.

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Postgraduate Clinical NOTES

12. MAMMARY CANCER

The best treatment for cancer of the breast is radical surgery with meticulous dissection of the adjacent lymph nodes. When the axillary glands are involved, about 25 per cent of women so treated live 5 years or more; when there are no metastases in the axilla, about 75 per cent of the women survive beyond 5 years.

Huggins, Charles: Progress in the treatment of advanced cancers. *The Merck Report*, April 1953, page 3.

Relation of Potassium to the Failing Heart and Digitalis Intoxication

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Potassium is essential to the functioning of the myocardium from which it is lost in pathologic processes, and to which it is restored by digitalis therapy. This important relationship suggests the employment of potassium salts as therapeutic agents in the management of heart disease.

D. A. J. MOREY

RECENT interest in potassium and electrolyte balance in the surgical as well as the medical patient and the detection of potassium imbalance by the electrocardiograph has refocused attention on the influence of potassium on cardiac function and its place in cardiac failure and rhythm irregularities.

This paper is a brief review of the literature on this aspect of the metabolism of the potassium ion, from which certain conclusions and recommendations are drawn.

Early Observations

In 1941 Stoll and Nisnewitz[1] observed that the serum potassium and the electrocardiographic T waves were depressed during attacks of periodic paralysis, with a return to normal levels following administration of potassium salts.

One year later Keith, Osterberg and Burchell[2] demonstrated that large doses of potassium chloride produced an increase in the serum potassium levels together with an elevation of the T waves.

In 1944 Brown, Currens and Marchand[3] presented reports on 2 patients with chronic nephritis who experienced episodes of flaccid paralysis of the extremities as a result of potassium loss in the urine, and these workers demonstrated associated electrocardiographic changes which they compared to the changes encountered with toxic doses of digitalis. These changes they were able to reverse by the oral administration of potassium chloride.

Similar findings were reported by Nicholson and Spaeth[4] (1949), who presented 4 cases of S-T and T wave changes associated with a low serum potassium. In each case they were able to restore the electrocardiographic deviations to normal when they restored the serum potassium to its normal level.

Prior to these studies Boyer and Poindexter[5] (1940) expressed their belief that the effect of digitalis on the heart muscle seemed quite similar to that of the adrenocortical extract which tends to maintain potassium within the cell. This opinion was supported by their studies on cats in which they showed that therapeutic doses of digitalis produced a significant increase in the intracellular potassium of the heart muscle. They pointed out that the skeletal muscle weakness caused by

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adrenalectomy and the myocardial weakness associated with cardiac failure are both accompanied by a decrease in intracellular potassium, and felt that the improvement in contractile power effected by the administration of adrenocortical extract or digitalis, respectively, may be related to the resultant restoration of potassium to the muscle cells where its presence is essential to the vital biochemical processes. This similarity of action between the adrenocortical hormones and digitalis is further supported by the striking similarity between their chemical structures.

Since these studies many workers have confirmed the fact that there is a loss of potassium from the body in cardiac failure which is roughly proportional to the extent of cardiac damage or hypertrophy.

A great deal of work has been done on the effect of digitalis on the chemistry of the heart muscle, and it has been demonstrated that carefully calculated therapeutic doses produce a uniform and significant increase in the intracellular potassium, tending to restore the concentration of this ion to its normal level. However, if these doses are increased to toxicity levels there is again a marked loss of potassium from the muscle cells, often accompanied by arrhythmias and S-T and T wave depression.

Thyrotoxicosis has been shown to produce a loss of potassium from the muscle cell which may be partially prevented by the administration of adrenocortical extract. This may explain the refractoriness of the failing thyrotoxic heart to digitalis.

Toxic Arrhythmias

Sampson and his associates[6] demonstrated how ectopic beats caused by digitalis intoxication could be abolished by the oral administration of potassium salts in doses of 5 to 10 gm. They presented evidence supporting the contention that potassium balance within the heart muscle is disturbed by the administration of digitalis in toxic doses. They further demonstrated, however, that there was no correlation between the presence or absence of ectopic beats and the fasting serum potassium level, for when the ectopic beats were abolished by the administration of potassium they failed to return in many instances until long after the blood serum potassium had fallen to the fasting level.

Buff[7] reported on 5 cases of intoxication with digitalis leaf; he treated these patients with oral potassium chloride and obtained excellent results both symptomatically and electrocardiographically. He observed that patients receiving this treatment became alert and cooperative, which he felt was in marked contrast to the results obtained by the use of the low sodium diet alone. He felt that the addition of potassium chloride to digitalis therapy not only enhanced the action of the digitalis but also delayed or prevented the onset of digitalis toxicity. His regimen was 5 to 6 gm. of potassium chloride by mouth for intoxication, followed by 1 gm. three times a day until a definite level of therapeutic digitalization had been achieved. Thereafter he recommended a maintenance dose of DIGOXIN® and 1 gm. of potassium chloride daily.

This administration of potassium salts should enhance not only the action of the digitalis drug employed but also the excretion of the sodium ions. Buff anticipated potassium intoxication in each of his patients, but this did not develop.

Enselberg, Simmons and Mintz[8] studied 31 patients with various arrhythmias, most of which were attributed to digitalis toxicity. These arrhythmias were ventricular extrasystoles, auricular tachycardia, auricular flutter and fibrillation. Forty trials were carried out in which from 2 to 10 gm. of a potassium salt was given orally. In each case clear effects were obtained, which appeared in half an hour and persisted for at least four hours. Ventricular extrasystoles were uniformly reduced or abolished. However, conduction disturbances in general were increased.

Stempien and Katz[9] presented a case of paroxysmal ventricular tachycardia in which there was no response to large doses of quinidine, magnesium sulfate, atropine or quinine; response was noted, however, after the third dose of potassium chloride was given (1 gm. every four hours). They re-

called a similar case reported by Sampson.

Biochemical Role of Potassium

The exact biochemical role played by the intracellular potassium is still unknown. However, its importance is apparent from these studies in which it has been shown to exert an influence on myocardial conductivity, excitability and refractoriness.

Conclusion

It is recommended that potassium be given a place in the current therapy and management of heart failure and digitalis intoxication (especially ventricular extrasystoles) and in conjunction with quinidine in the treatment of paroxysmal ventricular tachycardia.

Attention, however, is drawn to the need for an adequate urinary output to avoid the possibility of hyperpotassemia.

Summary

A review has been made of the experimental and clinical evidence related to the influence of potassium in cardiac dysfunction and digitalis intoxication.

It is believed that the failing myocardium loses potassium and is consequently weakened in a manner comparable to the skeletal muscle weakness encountered in familial periodic paralysis, Addison's disease and thyrotoxicosis.

Both the action and the chemical structure of digitalis have been likened to those of the adrenocortical hormones which are thought to be instrumental in returning potassium to the myocardial cells in order to restore the contractile strength to the muscle.

In the presence of digitalis intoxication, however, the process appears to be reversed and potassium is again lost or altered in such a manner as to produce cardiac excitability and conduction defects. Certain of these irregularities respond to potassium therapy.

Recommendations are made to include potassium in the therapy of heart failure, digitalis intoxication and paroxysmal ventricular tachycardia.

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7. Buff, I. E.: The use of potassium chloride and Digoxin in congestive heart failure. South. M. J. 42:1037, 1949.
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MEETINGS AND POSTGRADUATE COURSES

University of Minnesota: Continuation course in rehabilitation, for general physicians, October 22-24, at the Center for Continuation Study. Faculty will be headed by Dr. Donald L. Rose, University of Kansas School of Medicine, and the program will be under the direction of Dr. Frederic J. Kottke.

The Tulane University of Louisiana School of Medicine, Division of Graduate Medicine: Psychosomatic problems in general practice, November 16-21, Dr. Robert G. Heath, chairman.
Ocular pathology, November 30-December 5, Dr. James Allen, chairman.
Electrocardiography, November 30-December 11, Dr. George E. Burch, chairman.
Surgery, gynecology and traumatology, January 11-16, 1954, Drs. Alton Ochsner, Marshall L. Michel and Jack K. Wickstrom, chairmen.
Pediatric surgery, February 8-13, 1954, Dr. Ralph V. Platou, chairman.
Surgery of the hand, March 4-6, 1954, Dr. Jack K. Wickstrom, chairman.
Internal medicine for general practitioners, March 22-27, 1954, Dr. Robert Snavely and Dr. George E. Burch, chairmen.
For further information on the courses listed above, write the Director, Division of Graduate Medicine, 1430 Tulane Avenue, New Orleans 12, Louisiana.

Northwestern Ohio Medical Association: 109th Annual Meeting, October 14, 1953, at the Academy of Medicine, Toledo. Reservations may be sent to: Dr. Henry B. Larzelere, 1838 Parkwood Avenue, Toledo 10, Ohio.

Common Errors in X-Ray Diagnosis

FRED J. HODGES*

University of Michigan Medical School, Ann Arbor

A number of factors, both technical and clinical, operate to determine the over-all accuracy of x-ray diagnostic efforts. While repeated mistakes which stem from incorrect technic are not to be tolerated, those errors which represent well intended but incorrect clinical judgment are very difficult to control and sometimes are amusing.

FRED J. HODGES

ERRORS in roentgenologic diagnosis occur because of (1) failure to use roentgenographic methods sufficiently often and widely; (2) erroneous technic; (3) failure to recognize normal variants as such or to recognize deviations from normal, and (4) failure to translate x-ray signs into terms of clinical pathology and do it correctly. The latter is by far the greatest source of error.

By means of the accompanying illustrations, I shall try to show you a fairly wide range of situations which offer difficulty in diagnosis.

A very common mistake made by radiologists is illustrated in Figure 1. On the left is a normal roentgenogram of the chest of a young child. On the right is a film of the same chest made within a few seconds of the other, and the appearance is grossly abnormal. The difference represents the difference in phase of respiration. The chest on the left is in a phase of deep inspiration, whereas that on the right is in expiration. These films were made to demonstrate that failure to appreciate the fact that incomplete aeration has occurred is enough to send one off on a wild goose chase of nonexistent disease.

Figure 2 indicates how one can misinterpret abnormalities which are clearly obvious. The roentgenogram on the left shows a chest with abnormal density in the lungs hugging the cardiac shadow. Years ago this could easily have been called bilateral bronchopneumonia; it might have been mediastinal disease spreading into the lung on both sides. Actually, five days later the film shown on the right was made, and there is no such abnormality. This is explained by the fact that the patient's threatening cardiac failure had been handled properly and pulmonary edema has disappeared. The absence of normal aeration in the lung is the basis for recognition of abnormalities, and one must remember the multitudinous situations that can be produced by incomplete aeration.

Obvious pulmonary tuberculosis is illustrated on the left in Figure 3. The position of the lesions high in the upper lobe is quite characteristic, and with the use of stereoscopy the radiologist should be able to discuss the situation with the internist, who

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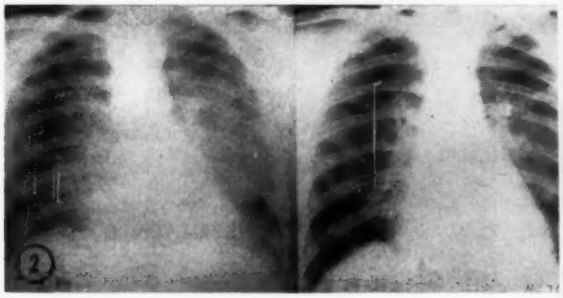
Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association in Cleveland.

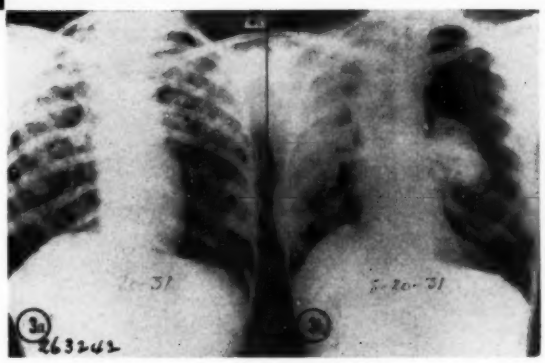


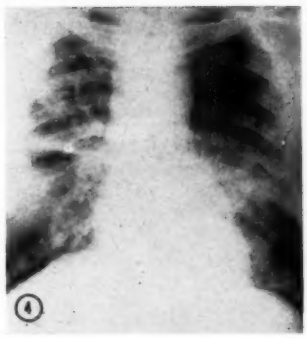
would then go about the usual methods of providing positive proof. On the right is a roentgenogram of the chest of the same patient; pneumothorax has been carried out on one side and ultimately was done on the opposite side, with recovery.

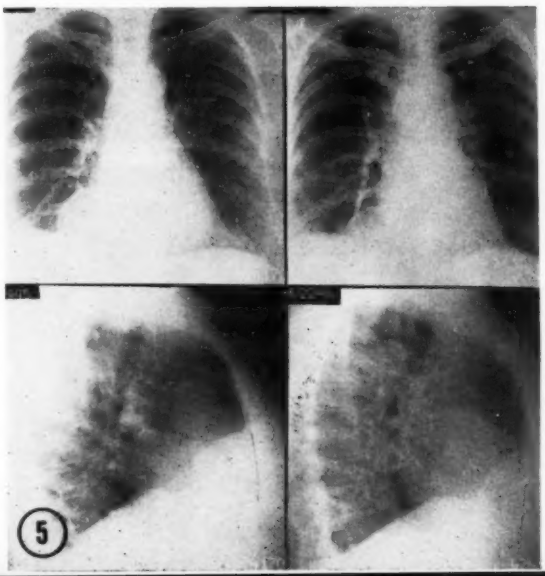
Very real abnormalities involving both sides of the mediastinum are illustrated in Figure 4. This is a situation that might well tax the radiologist's ability. The distribution is not characteristic of any particular disease. This patient was a miner from Michigan. At autopsy it was found that he had Hodgkin's disease with definite lesions in the lung, sarcomatous in type; he had silicosis and he had tuberculosis. In such an instance the radiologist is licked before he starts, and he must realize that this can happen to him.

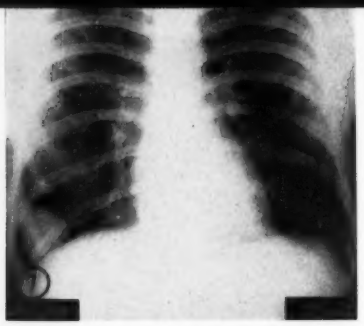
Figure 5 illustrates a trap which is a serious one—serious although often very simple. Of the four chest films shown, two are frontal and two lateral. Notice in the cardiophrenic angle on the patient's right there is a rounded opacity. What could it be? A rather common explanation, true in this case, is accumulation of pleural pericardial fat, sometimes removed by surgeons and very kindly called lipoma by pathologists. These fat pads are also very common at the cardiac apex, and there one is more likely to anticipate them. I have included two sets of films because I wanted you to see that a 50 pound weight loss has been associated with decrease in the size of the fat depot in the chest. The films on the right were made after the patient, formerly obese, had lost 50 pounds.

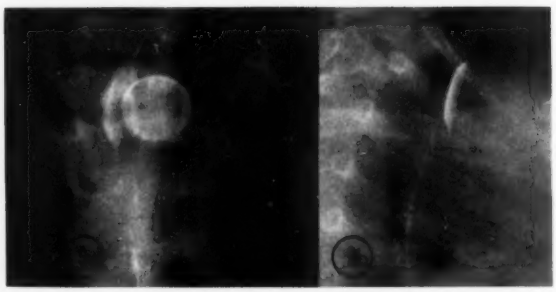
A very profound abnormality is obvious in the roentgenograms shown in Figure 6.





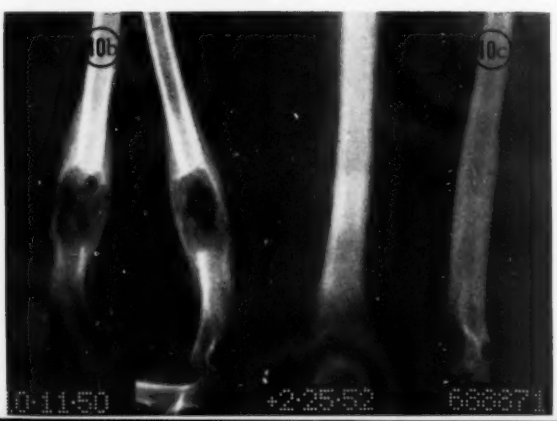






There is no doubt here that there is a deviation from normal, but what does it represent? It has a sharp edge and might well be encapsulated fluid. Actually, the ribs on the affected side are slender and wedge shaped. It was reported that the patient had café au lait spots on his skin. Well, what of it? Probably it is a neurofibroma arising from the posterior wall of the chest. Operation was carried out and the surgeons noted that the mass contained fluid. They searched until they found the stalk by which it was attached. This is an anterior meningocele communicating with the meninges in the spinal canal—a most unusual situation. We have seen 6 or 7 such cases, but in no case was the mass as large as this. So there I give you an error in x-ray diagnosis which is apt to be made again, I am afraid.

The abnormality in Figure 7 stands out in clear detail in the right base near the angle of the diaphragm and the chest wall. The patient, an 18 year old man, was rejected for military service because of this finding. Fortunately, he had been our patient when he was 5 years old. At that time he had been admitted to the hospital because of a large abdominal mass attached to the kidney which proved to be a Wilms tumor. During the 13 years which followed, we had either examined him every six months or kept in touch with



him by mail and obtained films. So we had a record showing that nothing abnormal had been noted in his chest during that time.

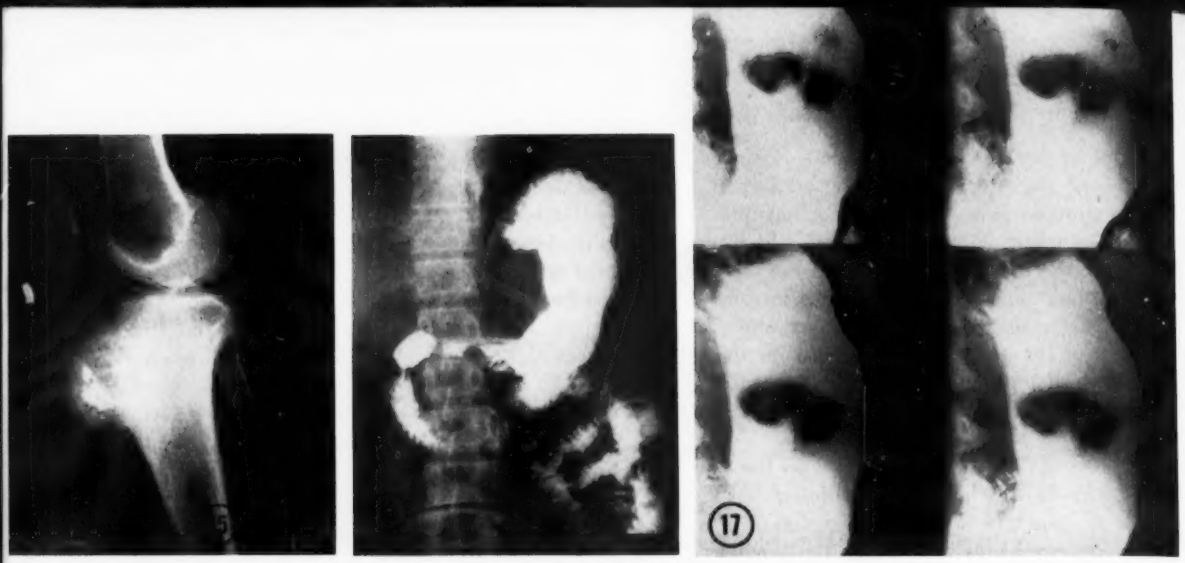
We asked ourselves, Could this be a metastasis at this late date? The lower lobe was resected. The tissue specimens matched—a Wilms tumor occurring 13 years after resection of the primary tumor. Without the very helpful background, the radiologist certainly could never have identified this lesion, nor should he have tried.

The obvious discoid shadow on the film in Figure 8a lies in the horizontal plane of the body; this tells the radiologist that it is within the esophagus rather than the trachea, and that it probably is a coin. The film in Figure 8b is the payoff, but the otolaryngologist didn't wait; he saw the first film, and promptly proceeded to remove a penny from the esophagus. He checked to see if there was any soft tissue trauma, and found another penny. He took it out, went back, and there was still another penny. As you can see in Figure 8b, a lateral view reveals a neat little stack of pennies. This is an instance in which a mistake arose because of incomplete, inadequate attention to the job and being satisfied with first glimpse impression.

The next case might be the same situation. You cannot fool the same old dog twice, of course, so this shadow lying parallel to the transverse plane of the body, discoid in shape, somewhat transparent and surrounded by a small amount of barium, is in the esophagus. In the lateral view, if you look closely you can see the air-filled trachea in front of the shadow and barium behind it. There is a little ear on this circular object. It isn't a coin. In the lateral view it looks as though it is depressed, as though it might be a thin foil of metal on cork, a part of a bottle stopper. But that doesn't account for the little ear. Actually this is a Red Cross button of the kind that is made without any pin but just a little turnover snap on the side to put on the lapel. We fed barium and noted that none clung to the object. It seemed as though it stood out in front of the esophagus. If a discoid foreign body lies in the trachea it will parallel the sagittal plane. If it is in the esophagus it lies horizontally. This Red Cross button had been aspirated two months before. It had gone down the trachea, sawed a hole through the membranous portion of the trachea and buried itself in soft tissues. The radiologist's sure-fire sign of an esophageal foreign body let him down.

In the field of bone diagnosis the radiologist has quite a time. He is asked, and quite properly, the nature of lesions, whether neoplastic or non-neoplastic; if neoplastic, whether they are primary, and if primary, whether they are benign or malignant. Such a problem involving the humerus is seen in Figure 10a. The abnormality is not completely midshaft but it is at a place where primary osteogenic tumor could well arise; there is destruction of bone cortex, and laminated new bone. We felt that this case had many earmarks of malignant primary bone tumor. You know as well as I the treatment that would have followed. We are very strong believers in biopsy, however, and Figure 10b shows that the surgeons removed a very sizable piece of bone in order to get an adequate and comprehensive biopsy. The pathologic report was not neoplasm but a traumatic bone cyst.

Figure 10c was taken three years later and shows perfectly healed bone with no evidence of disease. It is this sort of trouble that



a radiologist experiences in trying to make enormously important decisions. He knows full well that except in rare circumstances he has no right to say, "I am sure of this. It can't be anything else." Along with the others in the Tumor Conference, he is well aware that problems of this sort require biopsy.

Another bone problem is illustrated in Figure 11. This is a tibia with a destructive lesion of the cortex with some associated proliferative disease subperiosteally. This caught us napping. The patient was a child, and it was the first time anyone had told us that pediatricians had begun putting needles into the marrow cavity to get fluids into the baby. This is the end result of that operation; I don't think we will be caught again.

The roentgenogram in Figure 12, showing bones of the feet, might easily be a classic example of gout. The proper bones are involved, and the margin between bone and cartilage has been invaded. Closer inspection, however, saved us from making a mistake. Observe the phalanges of the fourth and fifth digits and you will note shrivelling of bone, which is quite characteristic of Boeck's sarcoid or sarcoidosis.

The next case (Figure 13) again brings up the question, What is it? Certainly there is disease in the lower end of the tibia showing eburnation of bone, some destruction of the inner surfaces of the cortex, and so on, but closer inspection will disclose a few very small white patches which represent sequestrums. We interpreted this to be a case of osteomyelitis, and that is what it turned out to be.

A similar situation is illustrated in Figure 14. I suppose it was guesswork, but we felt that the character of the periosteal new bone development in this case looked more ominous and that this was primary malignant neoplasm. I show these problem cases to illustrate how thin is the ground on which such decisions are made from x-ray evidence alone.

Another lesion in the upper end of the tibia is illustrated in Figure 15; there are bulging at the upper end of the bone and raylike projections extending out into the soft tissue mass. It is a textbook story of osteogenic sarcoma, and we thought that was what it was. Biopsy disclosed that it was benign chondroma, and it behaved as such after excision.

Let's turn briefly to problems involving the gastrointestinal tract. Figure 16 shows a barium-filled stomach with an intraluminal defect. Additional exposures proved this finding to be constant. It looks like an intraluminal neoplasm, but at operation it was found to be aberrant pancreatic tissue growing in the stomach wall. Radiologists make errors of this type in good faith, and I maintain that it is reasonably safe to report gastric neoplasm and not be the least bit embarrassed when it is discovered that this is not the case. The end results of primary gastric neoplasm are pretty gloomy, and to find that the diagnosis is erroneous is good news.

A lobulated defect in the stomach is shown

in Figure 17. There is a space-occupying mass, and an accumulation of barium doesn't move. This represents neoplastic tissue found at operation to be leiomyosarcoma and not, as we had supposed, gastric carcinoma.

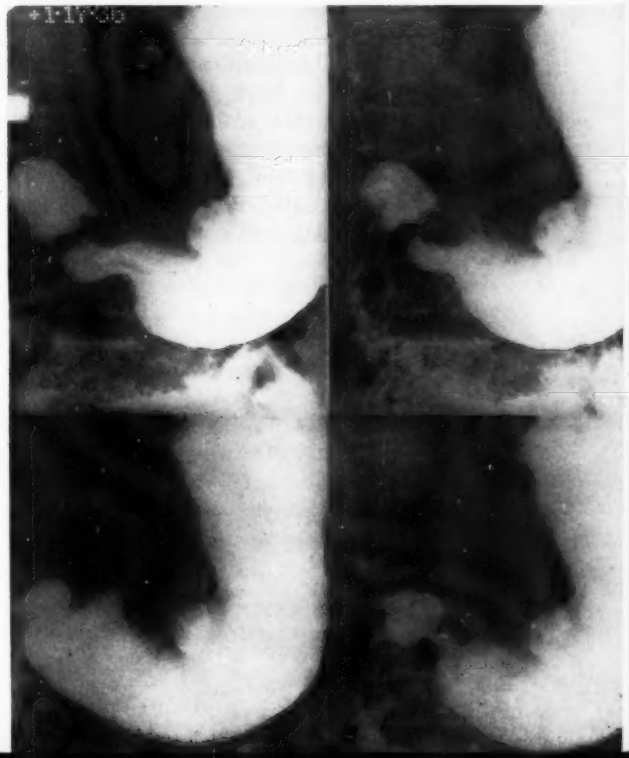
Next is a gastric ulcer on the lesser curvature (Figure 18a). There is nothing here to arouse the suspicion of malignancy in the mind of a radiologist. The criteria on which the diagnosis of malignant ulceration is based as compared with benign ulcerations are not very reliable, but they usually have to do with irregularity of ulcer margins or evidence of tissue growing into the base of the ulcer. We reported this to be a benign ulcer. In six weeks it had fully disappeared (Figure 18b).

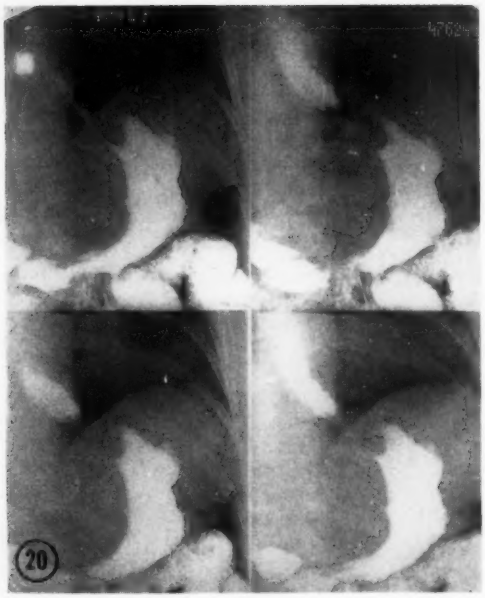
Three years later this patient was seen with gastric carcinoma encircling the stomach (Figure 18c). I cannot say that the original ulcer was malignant. If so, it should not have healed promptly. I am inclined to believe that the presence of gastric ulcer is not a very good insurance policy against the ultimate occurrence of primary gastric carcinoma.

Breaks in contour are a feature of the gastric ulcer shown in Figure 19. There seem to be small pegs of tissue sticking into the ulcer base. This, in all probability, is a neoplastic ulcer.

At operation it was found to be a gastric ulcer, and a large one, penetrating and perforating entirely through the wall of the stomach, eroding into the pancreas. The tissue masses at the base of the ulcer were pegs of pancreatic tissue. Ordinarily dependable criteria sometimes let you down when you are trying your very best.

Figure 20 shows persistent irregularity of contour involving the lower esophagus and the cardia of the stomach. This is an extensive carcinoma of the stomach extending into





the esophagus. My purpose in including this figure is to show depression of the gastric cardia because of interposed tissue between the cardia of the stomach and the dome of the diaphragm. Sometimes the only indication of gastric carcinoma is this separation between the cardia of the stomach and the crest of the diaphragm. Notoriously, lesions which occur in the uppermost end of the stomach are those which the radiologist is most likely to miss. On the other hand, he is far more apt to call lesions which are nonexistent at the lower end of the stomach, where they are more common.

The last illustration (Figure 21) is not a radiologic mistake, but a mistake which, in all fairness, should be borne by internal medicine. This patient came to me to be examined, with the clinical comment that his presenting symptom was dysphagia. He came into a greatly darkened room; I talked with him and called him by name; I asked him something about himself and didn't learn much, so I had the nurse give him barium. Dysphagia, my eye! I had to race with the fluoroscopic screen down as fast as I could, through the chest, through the abdomen and clear down to this man's knees. Figure 21 shows the femurs and a huge inguinal sac. The entire stomach was within the scrotum! Sometimes the highly touted clinical information so essential to a good x-ray diagnosis is really very disturbing.

Cutaneous Metastasis of Adenocarcinoma of the Rectum and Sigmoid

RAY H. BURNIKEL AND ROBERT T. McCARTY*

Marquette University School of Medicine, Milwaukee

Malignant tumors are characterized by their ability to form metastases. Adenocarcinomas of the rectum and sigmoid have this ability, and often the site selected is far removed from the original lesion. Two cases of cutaneous metastasis of adenocarcinoma of the rectum and sigmoid are presented, and the possible routes for their arrival at the site are discussed.

ONE of the outstanding characteristics of malignant tumors is their ability to form metastases. Often these metastases are far removed from the primary tumor, and the route and method of their development are often vague but always interesting. Adenocarcinomas of the rectum and sigmoid are lesions that will at times produce metastases at distant sites. Trimble and McGoon[1] reported an interesting case in which the primary tumor of the colon was resected three years after a metastatic tumor to the brain had been excised. Adenocarcinoma of the rectum with metastasis to Virchow's node has been reported by Greenfield.[2] This was a solitary metastasis and lends itself well to speculation as to why and how the cancer cells arrived at that point.

The subject of metastasis from carcinoma of the rectum and sigmoid has been covered very completely in two articles by Bacon.[3,4] His first article contained a table listing the site, the number of patients with metastases at that site, and the percentage in the group studied. There was no mention of cutaneous metastasis in either of the groups he reviewed. As one would expect, the principal site of metastases was the liver, with 40 per cent of the patients studied having metastasis to that organ.

Both of the patients we are presenting had cutaneous metastasis from adenocarcinoma of the rectum and sigmoid and likewise had massive invasion of the liver. The peritoneum was involved in 18.6 per cent of the patients in Bacon's study; one of our patients had peritoneal implants. The lung was invaded in 14.7 per cent of Bacon's patients; both of our patients had metastases to the lungs although in Case 1 it was a very small nodule. Bacon found that the inguinal glands, ovary and broad ligament showed metastases in 1.9 per cent, 1.3 per cent and 0.9 per cent of his patients respectively. Our Case 1 had metastasis to the ovary and broad ligament, while Case 2 failed to show any evidence of invasion of those sites. Case 2 did, however, have metastasis to the adrenal, which was present in 6 of 366

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cases in Bacon's second article. It is interesting that Bacon found the greatest number of primary tumors to be grade 2 (Broder's) in his first group, while the histologic grading in the second group was higher. We did not attempt to classify Case 1, but in Case 2 biopsy of the primary lesion showed adenocarcinoma, grade 3. It is our present feeling that grading of the primary tumor adds little of a constructive nature to the management of a given case, and may give a false sense of security if the grading is low.

In the past few years there have been several excellent articles relative to skeletal metastases from carcinoma of the rectum. Weston[5] reported a case with metastasis to the humerus. In 1930 Aufses[6] reviewed the literature on bone metastasis and added 8 cases. From his review we find that Curling in 1870 reported the first case of rectal carcinoma with bone metastasis. Aufses found that the sites of metastasis followed very closely the prediction of von Recklinghausen, based on his theory of periaxial stagnation of neoplastic cells. The bones having the most stress and strain will be the ones most likely to be the site of metastasis, and Aufses found the vertebrae and the femur most often involved.

The most recent report is that of Beskin and Atwood,[7] who reviewed the literature while presenting a case of solitary metastasis to the left fourth metatarsus from carcinoma of the rectum six months postoperative in a patient otherwise well. They summarized the subject of skeletal metastasis in an excellent and complete table.

Case Reports

Case 1—A 66 year old Negro woman entered the hospital January 10, 1952, with complaints of hypertension and rectal bleeding. The rectal bleeding came from a "hemorrhoid" that had grown rapidly in the preceding two weeks. There had been a slight change in bowel habit requiring the use of a mild laxative during the preceding five months. She had had rectal bleeding at intervals for 40 years, and had been given a series of injections for hemorrhoids in 1946. Six months before admission she had noticed slight rectal bleeding. There had been a weight loss of 18 pounds in the previous three months. Other history is not pertinent, no serious illness or previous surgery having been reported.

Results of the physical examination were essentially negative, except for the abdomen and rectum. The abdomen was rounded and moderately tympanitic, with the liver enlarged and palpable. The rectal examination revealed an irregular, pale, very firm, 2 by 2 by 3 cm. tumor to the right and posterior to the anal opening, with multiple external skin tags. On admission the hemoglobin was 49 per cent, the color index 0.81, and the red blood cell count 3,090,000. The white blood cell and differential counts were within normal limits. The urine showed a 1 plus albumin.

The patient was seen in the Proctology Department on January 11 with the following findings: *Inspection:* In the right posterior quadrant there was a 3 by 4 by 3 cm., pale, hard, perianal mass about 2 cm. from the anal margin. Large external skin tags were present in the right anterior and right posterior quadrants. *Digital:* The sphincter tone was normal. There was induration posterior and lateral to the mass, and a free area of tissue between the mass and the sphincter. *Anoscope:* Large combined hemorrhoids were found in the primary sites. *Sigmoid:* To the 25 cm. level, the mucosal pattern was normal. *Impression:* (1) perianal tumor—(a) fibrosarcoma, (b) squamous cell carcinoma, (c) squamous cell papilloma—and (2) large combined hemorrhoids with external skin tags. The patient mentioned an abscess which had been present a year previously and which had healed, leaving a hard lump. She insisted that the growth as seen had developed in the preceding three weeks.

A bone survey was done on January 11 and reported as follows: The lower thoracic and upper lumbar segments revealed no evidence of osteoblastic or osteoclastic metastases. The long bones likewise showed no evidence of changes consistent with metastatic carcinoma.

On January 16, under caudal anesthesia, the perianal tumor mass was removed with an electrosurgical knife. The gross findings at surgery were: a 3 by 3 by 3 cm., irregular

mass in the right posterior area, approximately 2 cm. from the anal verge, extending into the deeper tissue and toward the rectum. A small area of mucosa in the right posterior quadrant was retracted and appeared to have granulation tissue present. There was a small nodule palpable in the rectovaginal septum which had an extension in the direction of the tumor.

The pathology report on the perianal tumor excised January 16 was metastatic adenocarcinoma of the perianal tissues.

The patient's postoperative course was poor. She refused additional surgery and was very reluctant to have further investigative work performed. However, a barium enema was done on February 15 and reported as follows: (1) carcinoma at the junction of the sigmoid and descending colon and (2) partial large bowel obstruction. The patient was given two whole blood transfusions of 500 cc. each and a total of 3,900,000 units of penicillin. She developed bronchopneumonia and a large bowel obstruction and died February 24.

The report of the autopsy performed is as follows: Cause of death—bronchopneumonia. The primary lesion (Figure 1) was found in the upper sigmoid and measured 9 by 6 by 3 cm. There were no other polyps or growths noted in the gastrointestinal tract nor were the regional lymph nodes involved. Metastases were noted in (1) the liver, which was large and weighed 4000 gm., being largely replaced by neoplastic tissue; (2) left ovary—with involvement of an ovary we had to consider this a Krukenberg tumor, which is by definition involvement of ovarian tissue secondary to malignancy in the gastrointestinal tract; (3) left broad ligament—small nodule, 1 by 1 by 1.5 cm.; (4) rectovaginal septum; (5) peritoneal implants, and (6) lung—small nodule 0.5 by 0.5 cm.

Cattell and Mace[8] have reported metastasis to the penis from carcinoma of the rectum. In the case they presented the route of the metastasis was by direct extension. On first sight we considered this to be direct invasion to the perianal skin from a lesion in the rectum, but when examination showed no lesion in the rectum or the lower sigmoid this was dismissed, and before removal the impression was that we were dealing with a lesion arising from skin or its derivatives. The lesion (Figure 2) was movable and certainly cutaneous.

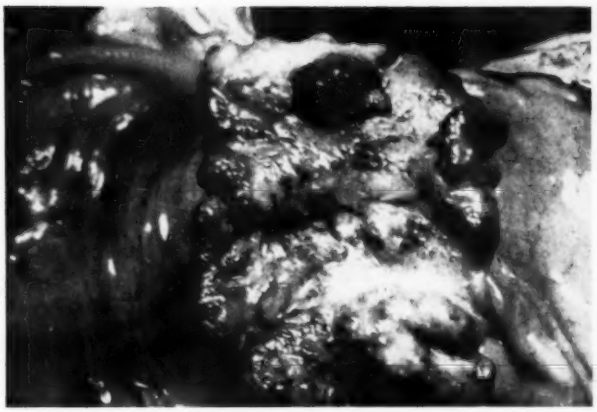

FIGURE 1 *(Case 1)*. Primary lesion in sigmoid.

FIGURE 2 *(Case 1)*. Perianal cutaneous lesion.

Charache[9] has reviewed the literature and presented 30 cases of tumors of the buttocks. Of his 30 cases, 12 were malignant. The malignant tumors consisted of the following:

neurogenic sarcoma, 7; epidermoid carcinoma, 2, and metastatic carcinoma, 3. In the group of 3 metastatic lesions the primary lesions were found in the kidney, intestine and malignant melanoma of the arm. He did not elaborate on these metastatic carcinomas, and we do not know in what part of the intestine the primary tumor was located. This is the only reference we have been able to find of a lesion comparable to the one we are presenting.

When the pathology report was received and the microscopic sections were reviewed we had to consider other possibilities. It had been established that we were dealing with metastatic adenocarcinoma. From the history obtained by the Proctology Department this patient had had what might have been an abscess about one year previously. McAnally and Dockerty[10] and Skir[11] have reported carcinoma developing in chronic fistulas. However, a review of the slides failed to show anything that could be interpreted as a chronic sinus or fistula. Consideration was given to the possibility of this being a primary carcinoma of an anal gland (as has been reported by Scarborough[12]) but again we could find no histologic support.

Case 2—A 63 year old white woman entered the hospital April 26, 1947, with the chief complaint of diarrhea of two months' duration. She had been well until two months previously, when she began to notice an increase in the number of bowel movements to seven or eight daily. Each movement was preceded by abdominal cramping and accompanied by pain on defecation. The stools were loose but normal in color. She never had noticed pus or blood in the stools. Symptoms had continued until the time of admission.

Her history revealed hypertension of four years' duration with epistaxis in December 1946; removal of a tumor from the uterus in 1931; menopause at the age of 47 with no postmenopausal bleeding; gravida I, para I; weight loss of 15 pounds during the preceding three months, and some frequency and nocturia during the previous three weeks.

Physical examination revealed a well developed, well nourished woman lying quietly in bed without distress. Her blood pressure was 190/104 and her head, chest and heart were normal. The abdominal configuration was globular with some increase in collateral venous circulation apparent laterally. The liver was 4 fingerbreadths below the right costal margin; the spleen was not palpable. A suprapubic midline scar was present.

Pelvic examination showed the presence of a cystocele and a rectocele. The posterior vaginal wall was involved in a hard mass which apparently originated in the rectum. Blood was oozing from the cervical stump. In the rectum a large, lemon-sized mass, tender to palpation, was located on the anterior wall. Impression—(1) carcinoma of the rectum, (2) hypertension and (3) cystocele and rectocele.

The patient was seen by the Proctology Department. A firm, fixed, semicircular, ulcerating, bleeding mass encircling two-thirds of the rectal wall was found at 3½ inches. The scope passed above the lesion, and mucosa above was normal. A biopsy was done (Figure 3) and the histopathologic examination revealed an adenocarcinoma, grade 3.

On admission the hemoglobin was 84 per cent, white blood cell count 8600, differential count normal, sedimentation rate 87 mm., urine negative, nonprotein nitrogen 31.9, and total and free protein 6.25—4.45—1.80.

The patient was prepared for surgery and on May 12 an exploratory laparotomy with a transverse colostomy was done. The carcinoma was found to be fixed to all the pelvic organs and a diagnosis of inoperable carcinoma of the rectum with metastasis was made. The liver contained numerous nodules varying in size from 2 cm. to 5 cm.

The colonic stoma was opened on May 19. The postoperative course was uneventful and the patient was discharged on May 28.

She was readmitted July 22. After leaving the hospital in May the patient had felt well and the colonic stoma had functioned well. There had been a 5 pound weight loss. Several weeks before returning to the hospital she noticed a lump in the left axilla and one on the anterolateral aspect of the left thigh. These masses were not painful and had not been in-

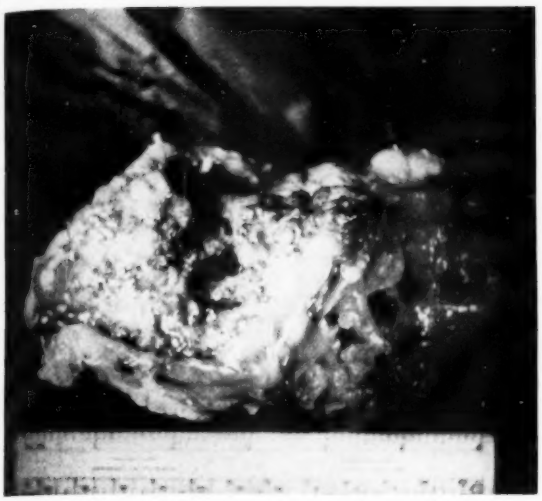

FIGURE 3 *(Case 2)*. Primary lesion in rectum.

creasing in size. On July 25, under a local anesthetic, the tumor masses were removed by blunt and sharp dissection and were found to be partially necrotic adenocarcinomas, which is compatible with a colonic origin. She was discharged July 27.

The patient was admitted to the hospital for the last time on December 1. She had continued to lose weight since July but had been fairly comfortable until the preceding two weeks when vomiting, which was periodic before, had become more severe. There was a 3 by 3 by 2 cm., red, firm tumor posterior to the right ear. It was not tender and had been present for three months. On the posterior aspect of the left side of the chest and overlying the midportion of the scapula, there was a 4 by 4 cm., raised, nontender, smooth tumor. The liver was palpable 2 fingerbreadths below the costal margin. Rounded, firm, reddened nodular masses, 6 by 4 cm., were located on the inner aspect of each thigh. The mass on the left thigh had been biopsied previously.

On December 26, under local anesthetic (1 per cent NOVOCAIN®), the colonic stoma was enlarged. The patient's course was gradually downhill with continued weight loss, increasing pain, and enlargement with breakdown of the cutaneous lesions. The patient died on April 14, 1948.

An autopsy was performed with the following findings:

Anatomic diagnosis—Carcinoma of the rectum was present with metastases to mesenteric lymph nodes, liver, left lung, scalp, left arm, right side of the chest, both thighs and the inguinal lymph nodes.

External examination—There was a soft, fungating tumor measuring 8 cm. in diameter over the right occiput just posterior to the ear. The center was ulcerating and measured 5 cm. in diameter. There was a small, firm tumor, 2 cm. in diameter and covered by normal skin, just posterior to the right breast. An ulcerating tumor just below the ribs and to the right of the midline was 2.5 cm. in diameter. The ulcer measured 1.5 cm.

There were several inguinal nodes bilaterally, which were firm and covered with normal skin, the largest measuring 2 cm. in diameter. A firm tumor over the biceps of the left arm, measuring 8 by 4 cm., was covered with normal skin and was freely movable.

A tumor of the left thigh just below the greater trochanter was cauliflower in appearance and measured 15 by 14 by 7 cm. It was freely movable and was not attached to the bone. A tumor of the right anterior midthigh measuring 15 by 16 by 5 cm. had several patchy areas of ulceration, the largest measuring 12 by 3 cm. Another tumor of the left thigh in the medial aspect just above the knee measured 9 by 7 cm. and was covered with normal skin.

Microscopic examination—Nine tumors were examined and the presence of adenocarcinoma of the rectum with metastatic adenocarcinoma of the lung, liver, adrenal, scalp, right thigh, anterior aspect of left thigh, right chest wall and medial aspect of the left thigh was established.

Case 2 presented no diagnostic problem. The primary lesion was easily found and biopsied, and a definite diagnosis established. The interesting thing in Case 2 was the development and progression of the multiple cutaneous lesions (Figures 4, 5 and 6).

Bacon,[13] in discussing metastasis, said:

FIGURE 4 *(Case 2)*. Cutaneous lesion, left knee.

FIGURE 5 *(Case 2)*. Cutaneous lesion, right thigh.

"The mechanism by which these cells reach or extend to new regions may be considered under the following headings: (a) direct continuity of structure (infiltration); (b) implantation or transplantation; (c) lymphatics and (d) blood stream." Direct continuity of structure was not considered as a mechanism of metastasis in either of these cases. Implantation or transplantation was not a mechanism in Case 2, but in Case 1 was considered. Certainly not probably, albeit possibly, a clump of cancer cells could have broken off the sigmoid lesion and moved down to get caught in an anal crypt, and then by direct extension to the perianal skin. One would be certain, however, in such a situation to find evidence on anoscopic examination, which was not the case.

The subject of the lymphatics and metastasis in carcinoma of the rectum and sigmoid is a large one. In 1931 Miles[14] gave us a classic description of the anatomy of the lymphatics of the rectum. He divided them into intramural, intermediary and extramural. The intramural lymphatics are in the wall of the rectum and consist of two networks, one submucous and the other between the muscular layers. The submucous is continuous above with the pelvic colon, and below with a similar network in the anal canal, and also with the lymph plexus in the subcutaneous tissue of the perianal skin. The intermediary also has two parts, the subserous where covered by peritoneum, and a lymph sinus where not. The extramural lymphatics are considered in three parts: (1) zone of downward spread, the structures in this zone being the perianal skin, the ischiorectal fat and the external sphincter muscle; (2) zone of lateral spread—involves primarily the levator ani muscle, and (3) zone of upward spread—most important in the spread of rectal cancer. Many of the mysteries of the spread of rectal carcinoma can be explained with the knowledge and use of this basic concept.

Gilchrist and David,[15] Gilchrist,[16] and Collier, Kay and MacIntyre[17] have done careful and exacting work on this subject of rectal carcinoma and lymphatic spread. They have washed, cleared, mounted and studied in minute detail the lymphatics in surgically removed specimens. Gilchrist and David[15] found that when a very careful search for lymph nodes is made about 68 per cent of all operatively removed specimens of carcinoma of the rectum will have metastasis to lymph nodes, and they pointed out that recognition of individual nodes by palpation is difficult or impossible if the nodes are small. In their series only 48 of 111 positive nodes showed any gross change, even in cross section. In a later article, Gilchrist[16] brought out several fundamental factors governing lymphatic spread of carcinoma: (1) Lymphatic spread progresses only when a node is completely loaded with cancer cells; (2) cancer cells do

FIGURE 6 *(Case 2)*. Cutaneous lesion, right occiput.

not completely destroy the function of a node until all of the node is destroyed; (3) cancer cells do not penetrate outside the capsule of a node unless there is a collection of involved nodes lying together; (4) lymph node metastasis has a common pattern; (5) spread is retrograde only if there is obstruction to lymph flow; (6) lymph nodes tend to block the spread of cancer, and (7) lymphatic spread of carcinoma is primarily embolic.

The findings of Collier, Kay and MacIntyre[17] were similar to those of Gilchrist and David.[15] They found that neoplasms on the anterior wall had a larger percentage of lymph node metastasis, and that the only lesions having involvement of lymph nodes along the lateral zone of spread were those arising between the mucocutaneous junction and a point 3 cm. above it. Black and Waugh,[18] and Glover and Waugh[19] added further to our knowledge of the retrograde lymphatic spread and the intramural lymphatic extension of carcinoma of the rectum and sigmoid in two later articles. That we had lymphatic metastasis in our cases is certain, but even after reviewing some of the fundamentals of lymphatic spread it is difficult to trace the route taken.

Blood stream transmission of neoplastic cells was a mechanism in both our cases. We worry a great deal about involved lymph nodes at the time of surgery for carcinoma of the rectum and sigmoid, and often fail to consider intravascular invasion. Brown and Warren[20] brought this out very clearly in an article written in 1938. They reviewed 170 cases of rectal carcinoma, 70 of which had visceral metastasis. Of these 70 cases, 61 per cent showed local intravascular invasion. Only 1 case of the 70 having visceral metastasis failed to show local intravascular invasion, but 24 of these cases failed to show positive nodes. They concluded that intravascular tumor invasion frequently means visceral metastases, and its absence nearly always rules out visceral metastases, so that its efficiency in predicting visceral or bone metastases outranks that of neoplastic lymph nodes. They presented a table listing the sites of metastases in their 70 cases, and mentioned that 2 had skin metastases, but did not elaborate on it.

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Therapeutic Agents in Hematology

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Some of the more important therapeutic advances in hematology are discussed. The indications for the use of liver extract, vitamin B_{12}, folic acid, iron, ACTH and cortisone, roentgen therapy, radioactive phosphorus (P^{32}), nitrogen mustard, triethylene melamine, the folic acid antagonists, and splenectomy are evaluated.

My purpose is to evaluate some of the recently introduced therapeutic measures in hematology. This branch of medicine is developing rapidly and it will be possible to discuss only some of the more important practical advances.

CYRUS C. STURGIS

First, I want to present 2 patients briefly. The first patient, Mrs. J., is 64 years of age. Four years ago, in 1948, when she was 60 years old, she came to St. Luke's Hospital in Cleveland complaining of loss of appetite, weakness, ease of fatigue, pallor, shortness of breath, and numbness and tingling of all four extremities. She told me just now that she also has experienced severe recurrent attacks of sore tongue during the past few years.

Here is a specific diagnostic picture that is important to remember. All the principal general symptoms of an anemia are present—weakness, ease of fatigue, pallor, shortness of breath and palpitation, plus recurrent attacks of sore tongue and numbness and tingling of all four extremities. I do not know of any condition other than pernicious anemia in which this combination of symptoms and signs occurs. Pernicious anemia, therefore, can be diagnosed with a fairly high degree of accuracy before the blood is examined.

The patient had three other important findings which corroborate the diagnosis, namely, achlorhydria, macrocytic anemia and megaloblastic bone marrow. Gastric analysis was done immediately following the injection of 0.5 mg. of histamine phosphate, which is the strongest stimulant we know to gastric secretion. A stomach tube was then passed and five or six specimens were removed at 15 minute intervals. There was no "free" hydrochloric acid in any of the samples removed. If "free" acid had been reported, despite the other characteristic findings, it would have cast considerable doubt on the diagnosis of pernicious anemia. Certainly if "free" acid had been found, the first thing to do would be to repeat the gastric analysis. If "free" acid were again found, then I would have to seek some other diagnosis. In general I do not approve of permitting one single labora-

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tory test to rule out all that I can learn from the history and physical examination, but such a finding would be strongly against the diagnosis of pernicious anemia. I have never observed "free" acid to be present in the gastric secretions in this condition, and it is my belief that the achlorhydria persists from birth until death in these cases.

Her hematologic changes were typical. There were 2,600,000 red blood cells per cubic millimeter and the hemoglobin level was 9.2 gm. or 59 per cent. The size of the red blood cells was not determined, but had they been I am certain there would have been a mean corpuscular volume of about 110 cubic microns as compared with a normal of 86 to 96. Sternal aspiration was done and many megaloblasts were found, which is characteristic of pernicious anemia; not more than 0.5 to 1.0 per cent of these cells are normally observed.

This patient, therefore, presents the typical findings of pernicious anemia and the diagnosis is established with certainty.

She was given 1 cc. of refined liver extract, 15 units, intramuscularly every day for a week; this was then continued twice weekly for a month—an excellent form of therapy. On the fifth day the reticulocytes of the circulating blood—the young red blood cells—showed a characteristic rise up to 20 per cent. In pernicious anemia in relapse and in normal persons, the reticulocytes make up 1 per cent or less of all the erythrocytes of the circulating blood. This characteristic increase occurs within two to three days after treatment is started and continues for about two weeks. When this response is present, we know the red blood cell count will become normal if efficient therapy is continued.

In 30 days her red blood cell count was 4,500,000 per cubic millimeter. This meant an increase of about 400,000 red blood cells per cubic millimeter per week, which is satisfactory evidence of efficient antipernicious anemia medication. The hemoglobin was 15.8 gm., or about 101 per cent, at the end of this period.

This patient has been observed for four years; she has done exceedingly well with continued maintenance treatment. All the symptoms, including the numbness and tingling, have disappeared, and she appears to be in excellent health. She receives, if I am reading the chart correctly, 15 units of liver extract every three weeks. In my opinion this is somewhat below the optimum dosage. I would give 15 units every two weeks, but many patients do well when receiving 45 units every six weeks as a maintenance dose. In general, 1 unit of liver extract or 1 micron of vitamin B_{12} given intramuscularly is a satisfactory maintenance dosage.

I should like to emphasize that this case illustrates three things about pernicious anemia. First, it represents the ease with which the diagnosis can be made in the typical case. When the condition is suspected in a patient with anemia, one asks, "Do you have numbness and tingling in the hands and feet?" To carry diagnostic weight, all four extremities must be involved. This type of paresthesia is present in 90 per cent of the patients with the disorder. The second question you ask is, "Do you have recurrent attacks of sore tongue?" Sixty-five per cent of these patients have this symptom. I have seen an occasional patient with pernicious anemia who did not have either of these complaints, but such a case is unusual. Then, of course, there are the blood findings, the results of sternal aspiration, the achlorhydria and the response to therapy, which make the clinical diagnosis of pernicious anemia highly accurate.

What is the optimum therapy of pernicious anemia? If I were treating such a patient with liver extract, in which we believe the only active material is vitamin B_{12}, I would calculate that 1 unit equals 1 mcg. of vitamin B_{12}. That is a satisfactory rule to remember. From 15 to 20 units (micrograms) should be given intramuscularly each day for the first week in the case of an untreated patient in relapse, and then 15 to 30 units (micrograms) twice a week until the blood is normal. This should be followed by 1 unit (1 microgram) a day thereafter as a maintenance dose. Fifteen units can be given every two weeks, or 30 units once a month, or 45 units every six weeks. Whichever dose is used, one

should be certain that the red blood cell count and hemoglobin are kept continuously within normal limits.

Probably vitamin B_{12} has only one advantage over liver extract. Both are complete forms of therapy for pernicious anemia; that is, they benefit the anemia, the tongue symptoms and the neurologic manifestations. The only advantage of vitamin B_{12} is this: I have never seen a patient become allergic to crystalline vitamin B_{12}, and a small percentage of all patients who are treated over long periods with liver extract will develop allergic manifestations varying from a slight stuffiness of the nose or mild urticaria to outspoken anaphylactic shock. Very rarely has a fatality resulted. Otherwise the two preparations are of equal value.

The next patient, Mrs. P., is 63 years of age. She came to St. Luke's Hospital in 1943, nine and a half years ago, when she was 54 years old. Her chief difficulty at the beginning of her present illness was inability to walk for a year before she came to the hospital. For about 10½ years thereafter, she was disabled for this reason. In addition, she had numbness and tingling of the hands and feet and symptoms which indicated a moderate anemia, namely, some weakness, ease of fatigue and shortness of breath. In brief, there was evidence of degenerative changes in the posterior and lateral columns of the spinal cord (indicated by her inability to walk) and some changes in the peripheral nerves (evidenced by the numbness and tingling of the hands and feet).

Pernicious anemia is characterized by a selective action on the spinal cord. The changes usually begin in the posterior columns of the lumbar region. In these columns are found the fibers exerting control of the sense of motion and position of the lower extremities. Also in the posterior columns are the fibers which are concerned with the vibratory sense. When Mrs. P. was first seen, ataxia was present because of degenerative changes in these posterior columns. Similar alterations had occurred in the lateral columns of the spinal cord which control the muscular contractions of the lower extremities. Hence her condition, when first observed, was an ataxic, spastic paraplegia, which is the characteristic finding in a certain number of patients with pernicious anemia.

In addition, a moderate anemia—2,600,000 red blood cells per cubic millimeter—was present and there was also a leukopenia which is characteristically present in relapse. An achlorhydria was found. The spinal fluid was normal, and the Wassermann, colloidal gold and Pandy tests were negative. The diagnosis was pernicious anemia with moderately advanced spinal cord changes.

Mrs. P. was treated very efficiently with concentrated liver extract given intramuscularly. Her blood was not restored to normal as rapidly as the previous patient's, but the red blood cell count rose to 4,000,000 per cubic millimeter in two months—that is, about 200,000 per cubic millimeter per week as contrasted to 400,000 in the other patient. Now her blood is in reasonably good condition but is not quite normal as the red blood cell count is about 4,070,000 per cubic millimeter. Her paralysis has not improved greatly. At least one can say that it has not progressed during the past nine and one-half years, which it undoubtedly would have done had treatment not been given. Although she can walk, assistance is necessary and there is obvious impairment.

While liver extract and vitamin B_{12} are effective forms of treatment for the anemia of this disorder, they do not always permit the regeneration of neurons, particularly when these have been destroyed for more than one year. We assume that changes which have been present for less than a year have destroyed the nerve sheaths and left the axis neuron intact. If you observe a patient with pernicious anemia who does not have spinal cord changes and treatment is such that the blood is kept entirely normal, you can be quite sure the cord changes will not develop. Furthermore, if a patient already has cord changes when first seen, and the blood is maintained at normal persistently, the cord changes will not progress. When they have been present for longer than one year, however, it is difficult to restore normal function,

as in the case of this patient, although some improvement may occur.

Folic acid is useful in the treatment of certain types of macrocytic anemia such as that seen in sprue and also the variety seen occasionally in pregnancy. Never should it be employed in patients with pernicious anemia as the sole form of treatment, because it does not benefit the neurologic manifestations, and some believe it may do harm. In rare instances, however, I have given it in doses of 5.0 mg. orally a day in conjunction with the proper dose of liver extract or vitamin B_{12}, if the red blood cell count in patients with pernicious anemia does not return to well within normal limits. Occasionally the erythrocyte count will rise only to a level of about 3.8 million per cubic millimeter and remain there with liver extract or vitamin B_{12} therapy. The addition of 5 mg. of folic acid a day will often cause it to rise to normal. An investigation of the patient's diet in such instances will often reveal a low intake, especially of protein foods, and a correction of this deficiency will often produce an equivalent or better effect than the addition of folic acid.

Use of Iron Medication

It has been emphasized repeatedly in recent years that (1) iron can be expected to give satisfactory results only when administered to patients with an iron deficiency, which is almost always due to chronic hemorrhage, and (2) the dosage of the metal must be adequate. For a number of years I have attained entirely satisfactory results by giving enteric-coated ferrous sulfate tablets, 0.3 gm. (5 gr.), three times a day before meals. If the desired effect does not occur within two weeks, the dosage is doubled. I have not observed that the addition of anything else, including copper, vitamins, etc., has ever enhanced the effect of iron alone when given in the proper dosage.

We now have a preparation of iron which can be given intravenously. It is the saccharated oxide of iron. Let me emphasize, however, that I advise the oral administration of iron in all instances in which this is possible. Occasionally, however, a patient who cannot tolerate oral iron because it upsets the gastrointestinal tract can be treated successfully with saccharated oxide of iron. A 5 cc. ampule contains 100 mg., and we give 50 mg. (2.5 cc.) the first day slowly intravenously, then 100 mg. in a 5 cc. volume every day thereafter until the total calculated dose is injected. One hundred milligrams of saccharated oxide of iron will raise the hemoglobin in an average adult about 4 per cent. Therefore, if a 40 per cent deficit is present in the hemoglobin of the circulating blood you would give a total dosage of 50 cc. or 1000 mg. of saccharated oxide of iron over a period of 10 to 14 days in order to bring the hemoglobin to 100 per cent.

This preparation of iron is also useful occasionally in the last trimester of pregnancy when the patient finds it difficult to take the medication by mouth. Parenteral iron is not ordinarily indicated, but when needed it can be given without difficulty if it is injected slowly.

Use of ACTH and Cortisone in Hematologic Disorders

ACTH and cortisone may be used in a variety of hematologic disorders with benefit, but rarely, if ever, do they result in a complete cure. These preparations, whose mode of action is still not understood, may inhibit or control in some obscure way the pathologic changes associated with a disorder until recovery results from a spontaneous cure or until some other therapeutic agent can become effective. Furthermore, the improvement which follows the use of these preparations demonstrates at least that the pathologic condition can be reversed, if only temporarily. If this can be accomplished there is hope that eventually a genuine cure may be discovered.

Our experience has indicated that ACTH and cortisone may be of varying value in the treatment of the following conditions: (1) idiopathic thrombocytopenic purpura; (2) acquired hemolytic anemia; (3) acute and subacute leukemia; (4) multiple myeloma; (5) the terminal stages of Hodgkin's disease; (6) Felty's syndrome.

Adult patients whom we have treated with

this form of therapy have been given a 25 mg. dose of ACTH subcutaneously every six hours or a 75 mg. dose of cortisone orally every six hours for about two weeks. All patients have been placed on a low sodium diet (800 mg. per 24 hours). No untoward results have been observed when this precaution was observed.

Idiopathic thrombocytopenic purpura—Our experience with a fairly large group of patients with idiopathic thrombocytopenic purpura indicates that either ACTH or cortisone will induce a remission within three or four days in more than 90 per cent of cases. This remission is characterized by a moderate to striking increase in the circulating blood platelets and a gratifying control of the bleeding manifestations. If treatment is continued for 14 days and then stopped, about 60 per cent of the patients will relapse within a few weeks. A second remission may again be induced by the same therapy, which renders splenectomy safer because the bleeding tendency is partially or completely controlled. Splenectomy has resulted in cure in about 80 per cent of our patients. In the group who have had long remissions with medical treatment alone, all are doing satisfactorily to date, but the threat of a relapse is always present. The longest we have observed a remission thus induced has been for two and one-half years, and the patient remains in excellent condition.

We have observed cases in which ACTH failed to induce a remission when cortisone had been effective, but the reverse never has been seen; in other cases, both have been ineffective and splenectomy has succeeded; in still others, splenectomy has been ineffective and cortisone has been successful. Our suggestion concerning the therapeutic management of idiopathic thrombocytopenic purpura is to give ACTH or cortisone in the dosage recommended for two weeks, and then "taper off" by decreasing the total original dose by 25 per cent each day. At least a temporary remission is induced in almost every case. If the patient relapses (about 60 per cent do), then a second course of medication should be given and splenectomy performed when the platelets are at a level at which bleeding is controlled. This is usually accomplished at a level of 75,000 platelets per cubic millimeter, but a higher level is desirable. If there is an increase in blood platelets and this continues after the medication is discontinued, then the patient should be observed at intervals and further therapy given as indicated. If a relapse does occur, splenectomy following another course of either ACTH or cortisone is the treatment of choice in a great majority of cases.

Acquired hemolytic anemia—Both ACTH and cortisone apparently inhibit the increased hemolytic process in acquired hemolytic anemia and cause a rise in the red blood cell count which may reach normal. These preparations have no effect on hereditary hemolytic anemia (hereditary spherocytosis), and there is no conclusive evidence at present that they are useful in the treatment of the secondary type of hemolytic anemia such as seen in Hodgkin's disease, chronic leukemia and various other conditions. In the idiopathic acquired type, however, good temporary results follow this form of therapy in practically all cases. In less than 20 per cent, however, does the condition remain under control when medication is discontinued. Occasionally a long remission or possibly a complete one results. In one of our patients in whom the disease had been present for three years and had been severe enough to require blood transfusions, treatment with ACTH for 14 days produced a prompt remission which is still present after three years. In this disorder, therefore, ACTH and cortisone are useful (1) to induce a remission as a preliminary to splenectomy and (2) as a means of producing a long remission and possibly a cure in a small percentage of cases. Finally, these preparations in some unknown manner also permit patients with this form of anemia to tolerate blood transfusions which in some cases are otherwise associated with severe hemolytic reactions.

Treatment of Leukemia

It has been observed that patients with subacute and acute leukemias may derive a great temporary benefit from the use of either

ACTH or cortisone. Good results, however, are attained in only about 10 per cent of adults and 25 per cent of children, as evidenced by favorable changes in the blood and bone marrow. In addition, there is worthwhile clinical improvement in a considerable number of cases. In one of our patients, 25 years of age, with acute myelogenous leukemia (300,000 white blood cells per cubic millimeter, of which 90 per cent were "blast" forms), a perfect remission was induced by ACTH; the blood and bone marrow returned to normal and all evidence of the disease completely disappeared for about eight weeks. Subsequently, two additional remissions were also produced, and in all, the patient's life was prolonged approximately six months. Certainly this form of therapy is useful as an adjunct to blood transfusions, antibiotic therapy and the folic acid antagonists.

In our group of patients who received folic acid antagonist therapy, usually in the form of AMINOPTERIN® (4-aminopteroylglutamic acid), temporary improvement occurred in about one-third. Similar improvement has been reported in about 50 per cent of children receiving this form of therapy. It is probable that some type of alternating therapy with the folic acid antagonists and ACTH or cortisone will be of maximum benefit in these patients. In adults, the dose of aminopterin which we employed was 2 mg. orally a day, for a few days, followed by 1.0 mg. or less a day thereafter. Caution should be used in administering the drug, as the difference between the therapeutic and the toxic dose is slight. The development of leukopenia, thrombocytopenia, intestinal bleeding or a sore mouth is an indication for omitting the drug and readjusting the dosage.

More recently, triethylene melamine has been found to be of benefit in chronic granulocytic and chronic lymphatic leukemia, Hodgkin's disease, and a fair proportion of cases of lymphosarcoma. It is advisable to give this preparation cautiously by mouth in doses of 2.5 to 5.0 mg. every other day until a total dosage of 12 to 25 mg. has been reached. The medication should then be stopped, as severe toxic manifestations may arise. If none develops in 14 days, the course may be repeated provided the white blood cell count is 5000 per cubic millimeter or higher and no toxic symptoms are present.

Nitrogen mustard is only moderately effective in patients with chronic leukemia, but it is of great value in the treatment of Hodgkin's disease. It is given intravenously in doses of 8 mg. well diluted with saline, every other day for three doses. Urethane has been used in the treatment of chronic granulocytic leukemia and multiple myeloma. It is given orally in 0.3 gm. enteric-coated tablets after meals. The dose of 0.3 gm. three times a day is gradually increased to a maximum total dosage of 3.0 gm. a day. Although moderately successful results have been attained, in my experience the drugs often cause unpleasant gastric complaints, and beneficial effects have been only moderate in both these diseases.

In the treatment of multiple myeloma I have usually employed roentgen therapy which sometimes has given prompt temporary relief of back pain and otherwise improves the patient's condition. When refractoriness develops to this therapeutic agent, I have turned to urethane or more recently to ACTH or cortisone. The latter has most commonly been administered orally in doses of 75 mg. every six hours for two weeks, followed by a maintenance dose of 75 mg. daily. A low sodium diet has been given concurrently with the drug to prevent the accumulation of edema.

A summary of the present day treatment of chronic leukemia may be given as follows: In patients with chronic myelogenous leukemia, the preferred form of therapy is total body irradiation or radioactive phosphorus (P^{32}). The effects are identical but the radioactive phosphorus is more convenient to administer, if it is available. When the patient becomes refractory to irradiation, ACTH or cortisone is used. In addition, of course, blood transfusions and antibiotics are employed as indicated. Patients with chronic lymphatic leukemia are treated with localized roentgen therapy, and finally with ACTH or cortisone when the refractory stage is reached. Folic acid antagonists and ACTH and cortisone therapy are useful in the treatment

of the acute and subacute leukemias.

Patients with Hodgkin's disease should be treated with roentgen therapy when symptoms arise. After becoming refractory to this therapeutic agent, nitrogen mustard is employed and additive beneficial effects may be attained. When improvement is no longer derived from these two forms of treatment, ACTH or cortisone therapy may be used. In one of my patients, a 16 year old boy, it finally became impossible to give further treatment with either roentgen ray or nitrogen mustard because of the severe reactions which resulted. After the patient was given cortisone in a preliminary dosage of 300 mg. daily and continued on a maintenance dosage of 75 mg. a day, both therapeutic agents could be used without the slightest reaction and great temporary benefit followed. His appetite became ravenous and despite the fact that he did not accumulate edema, he gained 42 pounds over a six month period.

Treatment of Polycythemia

The treatment of polycythemia vera is now on a satisfactory basis. Although the disease cannot be completely eliminated, highly effective control measures can be instituted. These often permit a patient to live a normal life for many years. For the immediate relief of symptoms, phlebotomy should be performed with the removal of 500 cc. of blood, followed by the removal of additional amounts, 250 cc. at a time, every other day, until the patient's hematocrit reading is in the vicinity of 50 to 52 per cent. Additional treatment should be with total body irradiation until the white blood cell count is about 5000 per cubic millimeter. Satisfactory results also follow the use of radioactive phosphorus (P^{32}) in an initial dosage of 5 millicuries intravenously, with a repeat dosage, often somewhat smaller, given in about one month. Frequently, once the blood has been lowered to a normal level by either of these therapeutic agents, no further treatment is needed for a year or more. Two of my patients remained in good condition without further treatment for about four years. The older form of therapy with phenylhydrazine is inferior to the modern methods of therapy outlined and is no longer recommended.

It should be kept in mind that 3 to 5 per cent of all patients with polycythemia vera spontaneously develop chronic myelogenous leukemia. In my opinion there is no evidence, as some have suspected, that irradiation increases the risk of this complication.

Indications for Splenectomy

Although splenectomy has been employed as a therapeutic procedure for many years, more recently the indications for its use have been clarified and some agreement has been reached concerning its value. In my opinion the operation is clearly indicated at an early age, i.e., during infancy, in all patients with hereditary spherocytosis. The results are excellent and the risk is slight. In patients with acquired hemolytic anemia, although benefit is derived temporarily from ACTH or cortisone, splenectomy is usually required eventually. The results in such patients are not perfect but the chance of a cure is about 60 per cent. The operation should not be urged until an observation period has indicated there is no tendency to spontaneous recovery.

All patients with idiopathic thrombocytopenic purpura in whom the condition persists despite a course of ACTH or cortisone therapy should be seriously considered for splenectomy. A period of observation should be allowed to be sure that spontaneous recovery is unlikely. The results of splenectomy have been good, as about 80 per cent of the patients have made a complete recovery. In Banti's syndrome the results of splenectomy are less satisfactory, as about 80 per cent of the patients with this condition have cirrhosis of the liver. However, great improvement may follow splenectomy and a shunt between the splenic and renal veins to relieve the portal stasis. If the syndrome arises from splenic vein hypertension secondary to stenosis in the portal vein system, this may be corrected by vascular therapy. The effects of "hypersplenism," namely, anemia, neutropenia and thrombocytopenia, present in patients with Banti's syndrome should be relieved by splenectomy.

Felty's syndrome, which is characterized by manifestations of rheumatoid arthritis, an enlarged spleen, leukopenia and a normocytic, normochromic anemia, may be improved temporarily by means of ACTH or cortisone medication. As is to be expected, these preparations control the arthritic symptoms to a great extent during the period of their administration. They also produce an increase in the neutrophil percentage of the circulating blood and in the total white blood cell count. In a small group of patients whom we have treated, however, the period of improvement continues only as long as the medication is given, there being a prompt relapse within a few days after medication is discontinued. A much more satisfactory result follows splenectomy, which should be given consideration as a form of therapy in all patients with this disorder.

Postgraduate Clinical NOTES

13. THE DEFINITION OF ALLERGY

ALLERGY affects 10 per cent of the population." "The teaching of allergy in our medical schools is not what it should be," so that "practitioners know little about allergy."

At the recent meeting of the American Academy of Allergy, Dr. J. Warrick Thomas, President of the American College of Allergy, gave an excellent discussion of these statements. At the same meeting, Dr. William B. Castle discussed some of the reactions which occur in the blood dyscrasias, and Dr. Chester S. Keefer discussed reactions from drugs. All of these reactions depend upon antibodies, and so can be correlated with "allergy."

. . . .

Quite obviously, it is not possible to separate the reactions of allergy from similar reactions which may occur in normal persons. The symptoms depend upon the development of antibodies, sometimes in the circulating blood and sometimes attached to cells. . . . The field is large. What we study in allergy is the reaction of the body to noxious agents of all sorts and in wide variety.

How shall we teach such a subject to young students? The "allergist" does, of course, need special knowledge. . . . On the whole, however, there are only a few of these special points, and they can be taught without too much difficulty in the departments of medicine, provided only that the instructor will appreciate their importance from both the theoretical and the practical aspects.

Meantime, the statement that allergy affects 10 per cent of the population should be explained. Does it apply only to "allergic individuals"—or does it include all of those who may sneeze, wheeze or itch from causes which are sometimes defined quite easily and other times defined not at all?

Editorial by F. M. Rackemann, *Journal of Allergy*, May 1953, page 273.

The Present Day Treatment of Rheumatoid Arthritis

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The present day treatment of rheumatoid arthritis accepts the fact that the cause of this constitutional disease is not known. Therapy is not based on any single measure of treatment, least of all on any single medication given orally or by injection. The measures employed are drawn from the disciplines of physical medicine, orthopedics and internal medicine, and are carefully adapted to the needs of the individual patient. While special measures are applicable in selected cases, the program of treatment must be founded on careful attention to all factors which have an effect on general health.

WILLIAM D. ROBINSON

BEFORE we go into the details of the various aspects of management of rheumatoid arthritis, I think it is important that we have clearly in mind the present day concept as to what this disease is. It can be defined as a disease of unknown etiology, and as a constitutional disease. It is characterized particularly by a proliferative reaction in the joints and by spontaneous flare-ups and remissions.

Table 1 emphasizes briefly its characteristics as a constitutional disease. Clinical features such as fatigue and weight loss are present in a majority of cases. Laboratory evidences of its constitutional nature are the accelerated sedimentation rate found in virtually all cases; anemia, which is very common, and alteration in the plasma protein pattern, which may not be demonstrable by the usual clinical methods but is readily apparent if more refined methods such as electrophoretic determinations are used. These alterations consist of a decrease in albumin, an increase in the globulin fractions, particularly the alpha and gamma globulin fractions, and an increase in fibrinogen. Leukocytosis and fever are uncommon, but may occur.

During the last few years the investigation of tissue pathology of this disease has also indicated that rheumatoid arthritis is a generalized disease of connective tissue. In addition to the rheumatoid nodules which are noted in about 20 per cent of the cases, there is a frequent finding of inflammatory foci in the connective tissue between the muscle bundles and the nerve bundles.

However, the dominant feature of the disease is the joint involvement, the outstanding

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TABLE 1

CONSTITUTIONAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Clinical
Ease of fatigue
Weight loss
Fever
Rheumatoid nodules
Pathologic
Inflammatory foci in connective tissue, perimysial and perineural
Laboratory
Accelerated sedimentation rate
Anemia
Altered plasma protein pattern
Leukocytosis

characteristic of which is inflammatory reaction in the synovial membrane. As long as the inflammatory reaction is essentially exudative, with formation of fluid, outpouring of cells and increase in joint fluid, the process is essentially reversible. The outstanding feature of rheumatoid arthritis which differentiates it from other types of inflammatory arthritis is the proliferative phase of the granulation tissue reaction, with the development of fibroblastic and angioblastic proliferation and the growth of granulation tissue as a pannus over the cartilage, leading to cartilage destruction. It is this capacity of rheumatoid arthritis which leads to destruction of cartilage and development of scar tissue, resulting in fibrous or bony ankylosis.

With this concept in mind, it is easy to define the objectives of management of rheumatoid arthritis. The first of these is to control the general constitutional features and the inflammatory joint reactions in order to minimize joint damage. The second objective is to maintain function of the joint insofar as possible.

I would now like to describe briefly 2 patients whom Dr. Scherbel of the Cleveland Clinic has been kind enough to make available to us for this discussion. Mrs. S. is 56 years old and has had rheumatoid arthritis for 4 years. At the onset, the joints primarily involved were the wrists and the feet. Although she has had some remission, she has not been completely free of arthritis since its onset. For about 9 months dating from April 1951, following a 4 week course of ACTH therapy, she was relatively well, was able to get about and to do pretty much as she wanted. In view of our over-all experience, Mrs. S. was fortunate in having a relatively prolonged remission following ACTH therapy.

Her present difficulty involves particularly the knees, especially the left knee, which started bothering her in January 1952. There is a flexion contracture, and she has been unable to extend it completely or to walk without assistance since about April or May. She had no particular benefit from a course of cortisone therapy in May and June 1952. She has had some intermittent fever and has lost about 15 pounds.

There is typical involvement of the proximal interphalangeal joints, with obvious limitation of motion and of ability to make a fist.

In evaluating the functional status of these patients it frequently is important to evaluate their muscular strength, because muscle weakness is often as important as joint pain in the production of disability. Mrs. S. does not have a very tight grip, but does have good strength as far as the use of the thumb against the open palm is concerned.

She is particularly disturbed about her left knee, which has about a 25 to 30 degree flexion contracture. It is definitely warm and swollen, with a good deal of muscle atrophy.

(To the patient): I would like to ask you to lift up this knee. Can you hold it up if I take my hand away?

PATIENT: No.

DR. ROBINSON: The quadriceps femoris is the important muscle to maintain in order to eliminate a flexion contracture of the knee. While the knee can be straightened out with relatively simple orthopedic measures, in order to keep it straightened Mrs. S. has to learn to use her quadriceps muscle again.

Mrs. P., the other patient, also has had rheumatoid arthritis for 4 years. She had a relatively acute onset at the age of 31, 4 years ago, with fever and considerable weight loss. Her fever was as high as 100° to 101° F.,

and she had a slight leukocytosis. While the textbooks emphasize the insidious onset of rheumatoid arthritis, we have to appreciate that there are atypical forms of onset and that acute onset is not unusual.

She received treatment, and after 3 to 4 months experienced a virtually complete remission as far as her joints were concerned. I think we have reason to believe that her disease was not completely quiescent, because during this time she did have progressive difficulty in moving her elbows, and she has had virtually an ankylosis of her elbows for 2 to 2½ years. However, she continued to get along quite well until about 4 months ago.

She had her first baby in March 1952. She felt unusually well during her pregnancy, and quite well until about 3 to 4 months after delivery. Since then her primary difficulty has been involvement of the ankles, feet and knees. She shows very definite evidence of inflammatory activity in the knees, and also a slight tendency toward flexion contracture, but she is able fully to extend her leg against gravity. She has good quadriceps function, and a part of her treatment at present is to maintain that quadriceps function in order to prevent deformity at the knee joint.

(To the patient): How much weight have you lost since this last flare-up?

PATIENT: About 8 pounds.

DR. ROBINSON: Have you had any fever with this flare-up in the last 3 or 4 months?

PATIENT: Not that I know of.

DR. ROBINSON: Have you been tired?

PATIENT: To a degree, yes.

DR. ROBINSON: I think these 2 patients illustrate very well the evidence of constitutional involvement and some of the problems in management of the active inflammatory phase of the disease. Both have markedly elevated sedimentation rates. Mrs. P. has a very definite anemia with a hemoglobin of 8 gm., a red count of 3.7 million, and a hematocrit of 30 per cent.

The very fact that there are so many different methods in the management of rheumatoid arthritis is evidence that no single one is entirely able to give the desired results. In discussing the different methods of treatment I will arbitrarily classify them into 3 categories: (1) those of proved value; (2) those of probable value, and (3) a group which can be considered of questionable value in light of our present information.

TABLE 2

TREATMENT METHODS OF PROVED VALUE IN RHEUMATOID ARTHRITIS

Rest
Relief of pain
Physical therapy
Prevention and correction of deformity
Attention to general health
Nutrition
Anemia
"Focal" infections
Endocrine imbalance
Psychotherapy

Table 2 summarizes those methods which we feel should be regarded as being of proved value and which in general constitute the backlog of treatment in rheumatoid arthritis, regardless of what special measures may be popular at a given time.

First, rest is important; this means both constitutional rest and rest of the joints. It must be adapted to the individual, because certainly the patient with severe constitutional symptoms, fever or active inflammation of weight-bearing joints (such as the 2 patients presented) must have bed rest until those manifestations have subsided. In contrast, when dealing with a patient who has relatively few constitutional symptoms and involvement primarily in the fingers, we attempt to increase rest, but we have to make some compromise between what might be the ideal of sanatorium treatment and the practical exigencies of making a living. Even in those patients you can usually work out a pattern wherein the amount of rest can be increased to at least 10 and if possible to about 12 hours a day.

Second in the list are measures to relieve pain. This is an important end in itself, but also important if we are to attain two other

objectives: (1) to obtain rest and (2) to permit the patient to take care of the joints. For relief of pain we rely heavily on salicylates and in general feel that the lowly aspirin tablet is as satisfactory as other measures which have been suggested and have enjoyed popularity from time to time as substitutes. The currently popular substitute as an analgesic is phenylbutazone (BUTAZOLIDIN®), a new synthetic derivative which many of you may have had the opportunity to use. We have had the chance to work with the material for somewhat over a year and we feel that it is a satisfactory analgesic which occasionally may be superior to the salicylates. We also feel that it definitely has toxic potentialities and should be used only under careful supervision.

Physical therapy is an important part of the management of rheumatoid arthritis. Time permits me to point out only a couple of important principles: (1) that the therapy has to be adapted to the general condition of the patient as well as to that of the individual joints, and (2) that, in general, what you can teach the patient to do for himself at home day after day, or several times a day, is much more important than what can be accomplished with a short period of hospitalization. It is primarily a matter of educating the patient in simple measures of home physical therapy: the use of contrast baths and finger exercises, of paraffin baths and finger exercises, which they do two or three times a day at home; the use of an infrared lamp over the knees, or a baker, with quadriceps exercises; the use of contrast baths to the feet. These are methods of meeting common problems with respect to physiotherapy, with emphasis on the patient's carrying on over a long period of time.

The prevention and correction of deformities take us from the field of physical medicine into that of orthopedic surgery, and here, as usual, prevention is much simpler than correction. Even in the early phases of active rheumatoid arthritis, orthopedic principles may be applied with respect to splinting of joints, using cock-up splints for the wrist, a dynamic type of splint if there is a tendency toward the development of flexion contracture (this might be useful in the second patient at the present time), or perhaps a light plaster mold which is used at night. The splints are not left in place for a period of weeks; they are used essentially as molds and combined with exercise and physical-medical measures.

With respect to correction of deformity, much can be accomplished even in the presence of active disease. In the first patient whom we saw today with the flexion contracture of her knees, if the inflammatory phase of her disease can be brought under control the actual mechanical correction will not be too difficult. The long-range prognosis with respect to that knee depends largely on how well she carries out a long-range program of muscle exercises to maintain the knee in a good position.

The other measures listed in Table 2 are those which can best be summarized as attention to everything that bears on general health. They must be carefully adapted to each particular patient. There are some things that are so common that we check them routinely, but they do not necessarily apply in every case. Loss of weight is so common in these patients that they usually need a high calorie, high protein diet with liberal vitamin supplements. Some patients are overweight, however, and a reduction diet may be indicated.

The anemia, which is very common, can be approached by direct measures of treatment. Studies of the anemia of rheumatoid arthritis suggest that it has the characteristics of anemia of infection, and we would not expect it to respond to iron; however, a fair number of patients, particularly women, will have improvement with iron. If not, we tend to use blood transfusions quite liberally.

It is under this heading of attention to general health that we feel the matter of focal infection belongs at present. Patients should be checked for foci of infection; if these are found, they should be adequately treated, not with the expectation that you will cure the disease but rather with the expectation that you are removing one of several factors which have a deleterious influence on the general health of the patient.

The same is true with respect to use of en-

docrine preparations, particularly thyroid and estrogens. They are used if indicated in the particular patient, not as a specific method of treatment.

If we use the term psychotherapy in the broadest sense—giving the patient a definite program to follow, giving encouragement, and also using medication which may carry a suggestive factor—certainly it plays an important part in over-all management.

TABLE 3

TREATMENT METHODS OF PROBABLE VALUE IN RHEUMATOID ARTHRITIS

Foreign protein
Gold salts
Blood transfusions
Climate
Roentgen therapy (spine only)
Cortisone and ACTH
Intra-articular compound F

Table 3 summarizes briefly the methods we consider as being of probable value in the management of rheumatoid arthritis. We will spend some time later on some of these which are somewhat controversial. None of these measures can be relied on to bring about what can be termed a cure. They may accelerate the induction of remissions, and I think that is all we can feel that we are doing.

The use of foreign protein therapy, such as typhoid antigen, to produce fever has a definite place in selected cases.

The use of gold salts, the soluble gold salts, we feel still is of definite value in rheumatoid arthritis, again in selected cases.

Blood transfusions will occasionally result in more benefit than can be accounted for by correction of anemia, and for that reason our use of blood transfusions in these patients has been considerably more liberal in the last few years.

The matter of climate is a controversial one. We have placed it here as being of probable value. In advising change of climate, you can usually tell patients with rheumatoid arthritis that, other factors being equal, if they can take as good care of themselves in a warm, dry climate as they can at home, they probably will be somewhat better off. However, a change of climate cannot be expected to cure rheumatoid arthritis.

The rest of the agents listed in Table 3 have a relatively restricted field of usefulness. X-ray therapy in our experience has been the best symptomatic treatment for rheumatoid spondylitis (spondylitis rhizomelica, Marie-Strümpell arthritis). We have no evidence that it affects the course of the disease in the long run. It is our feeling that x-ray therapy is of no significant value in rheumatoid arthritis of the peripheral joints.

We have gone through a period of enthusiasm with respect to ACTH and cortisone and have been discouraged with the long-range results of management with these agents in an attempt to suppress the disease process. Again, in a restricted field there may be usefulness as far as the intra-articular injection of hydrocortisone or compound F is concerned.

TABLE 4

TREATMENT METHODS OF QUESTIONABLE VALUE IN RHEUMATOID ARTHRITIS

Vaccines
Massive dosage vitamins
Sex hormones
"Mysteroids"
DOCA® and ascorbic acid
Epinephrine
Para-aminobenzoic acid
Prolonged fever therapy
Muscle-relaxing agents
Sulfonamides
Antibiotics
Sulfur
Iodides
Bee venom

Table 4 lists a group of remedies which we would regard as being of questionable value in rheumatoid arthritis. The list could be extended indefinitely. I just want to indicate that with respect to vaccines, if they have any

TABLE 5

GOLD THERAPY FOR RHEUMATOID ARTHRITIS

Indication

Progressive or persistent activity despite adherence to conservative program

Contraindications

Uncertain diagnosis
Kidney disease
Liver disease
Previous sensitivity

Toxic Potentialities

Dermatitis
Stomatitis
Hepatitis
Albuminuria and hematuria
Bone marrow depression

Preparations

Gold thioglucose (SOLGANAL B®), 50 per cent gold
Gold sodium thiomalate (MYOCRISINE®), 50 per cent gold

Route

Intramuscular, at 5 to 7 day intervals
First dose, 15 mg.; second dose, 25 mg.; third dose, 50 mg., continuing until total dose is 800 to 1000 mg. Then interval between injections at 50 mg. level increased to every 2 weeks until total dose is about 1400 mg. May continue at 3 or 4 week intervals at same dosage level.

Precautions

1. Before therapy, determine the presence of satisfactory kidney and liver function.
2. During therapy, make weekly analysis of urine, including sediment; hemoglobin and white blood count; question for pruritus, rash, sore mouth. Every month, do a complete examination and a complete blood study.
3. Observe for any untoward effect; if noted, discontinue gold.
4. For definite toxicity, ACTH, BAL, antibiotics.

value it probably is a mild foreign protein effect. The use of massive doses of vitamins, particularly vitamin D and more recently B_{12}, is of very questionable value in rheumatoid arthritis. Following the announcement of the dramatic effects of cortisone, interest was aroused in large doses of the sex hormones, and then also in a group of steroids with no known or demonstrable metabolic activity which Dr. Hollander has dubbed the "mysteroids" (particularly pregnenolone and derivatives), which generally have no place and certainly cannot be relied on as specific measures of treatment even for relatively short periods of time.

I would like to discuss briefly three of the methods which we have classified as being of probable value, because they are controversial. I am sure there are differences of opinion with respect to where they should be placed in the over-all setup of the management of rheumatoid arthritis.

Table 5 summarizes our use of gold in the management of rheumatoid arthritis. We feel ideally that patients should be handled on a conservative program, utilizing the measures included in Table 2 and with attention to everything that bears on general health, for 2 or 3 months. Many patients, particularly in the early stages of rheumatoid arthritis, will do very well on such a program. No additional measures which carry the risks of undesirable effects need be considered. But in patients who have progressive or persistent activity of their arthritis in spite of an adherence to a conservative program, we think the use of gold should be considered. A history of previous sensitivity to gold is probably the chief contraindication. Uncertain diagnosis is definitely a contraindication, because gold is not of value in many forms of arthritis which can be confused with rheumatoid arthritis. The toxic potentialities should not be underestimated, but with our knowledge of the pharmacology of gold we can use it much more intelligently and considerably more safely than was true when it was first introduced in this country 10 or more years ago.

The severity of toxic reactions seems to be correlated with the magnitude of the individual dose more than any other factor, and the maximum individual dose is 50 mg. We follow a schedule at 5 to 7 day intervals, using only the soluble gold salts, thioglucose or thiomalate, and increasing the third dose to 50 mg. and continuing at that level until 800 to 1000 mg. has been given. The other modification which we have used for the last 5 years or so is tapering off instead of stopping

TABLE 6

LONG-TERM ACTH AND CORTISONE IN RHEUMATOID ARTHRITIS

	INITIAL	3 MONTHS	6 MONTHS	9 MONTHS	12 MONTHS	18 MONTHS	24 MONTHS AND MORE	TOTAL
Maintenance treatment	35	30	28	23	17	9	6	8*
Inadequate control		5		5	4	3	1	18
Peptic ulcer			1			2†		3†
Osteoporosis					1	2†		3†
Treatment-free remission			1		1	1	1	4

*Two patients have been on maintenance therapy less than 24 months.

†One patient had both bleeding ulcer and osteoporosis.

abruptly. The dosage is kept at the same level, but the interval between injections is increased to 2 weeks and later to 3 or 4 weeks. This has definitely not increased the frequency of toxic reactions and does seem to eliminate some of the relapses in patients who had initial good responses to gold.

Definite precautions are necessary with the use of gold, and we like to have evidence of good liver and kidney function before treatment is started. We check the urine carefully each time, including a check for red cells, because hematuria may be manifest before albuminuria. We check for any evidence of skin reactions or of blood or bone marrow depression. If there is any untoward reaction we usually stop the gold and observe the patient, because with few exceptions, severe reactions, particularly exfoliative dermatitis, occur in patients who have had mild manifestations of intolerance and in whom the treatment has been continued.

Until a few years ago if we got into trouble with gold we had no very satisfactory way of combatting gold toxicity. With the development of British anti-lewisite (BAL) we have a method of getting rid of gold in the body rather rapidly. Also, the results of treating reactions, particularly in the skin, with ACTH have been very satisfactory. Of course, the most feared complication is bone marrow depression, and certainly any evidence of this is a contraindication to further use of gold.

When ACTH and cortisone became available, their remarkable temporary beneficial effect on the disease process and the equally remarkable relapse as soon as they were stopped led to several attempts to use these agents as practical measures in the management of rheumatoid arthritis. One line of approach was with intermittent treatment—a 4 to 6 week course of therapy followed by a rest period, then another period of treatment, etc. This in general produced a succession of exacerbations and remissions with no tendency toward general improvement.

More than 2 years ago we started to approach this problem in a little different manner, namely, maintenance treatment. We tried to adjust the dosage in each case to a point where the symptoms were suppressed to a worthwhile degree without overdosage manifestations. Table 6 summarizes our experience over this period. Of 35 patients started on this program, a total of 8 are continuing on treatment at present. For these we have been able to find a dose that provides worthwhile improvement without untoward effects. In only one patient was a treatment-free remission of more than 3 months obtained without resorting to other methods of treatment when hormones were discontinued.

I call your attention to the very serious complications that have occurred in some of these patients, and particularly to the period between the ninth and the eighteenth month when in many cases arthritis became more and more prominent on a dosage which pre-

TABLE 7

INTRA-ARTICULAR COMPOUND F-ACETATE IN RHEUMATOID ARTHRITIS

	NO RESPONSE	INITIAL BENEFIT, LATER LOST	SUSTAINED BENEFIT WITH REPEATED INJECTIONS
Patients	6	3	16
Joints	8	5	30

Average duration of benefit, 7 to 10 days.
Maximum duration of benefit, 4 to 6 weeks.
Average dose, 25 to 37.5 mg.

viously had been quite adequate to control it. This I think has been quite a general experience with both ACTH and cortisone. In this group of patients about half received cortisone and half received ACTH. While this is a relatively small group, there probably are not more than 20 to 25 per cent of patients with rheumatoid arthritis in whom the use of maintenance treatments with these hormones constitutes a practical answer to their disease.

At present we are administering ACTH or cortisone initially only in those cases in which we can plan to use it for a definite period of time—to facilitate a certain step in the rehabilitation process, such as controlling the inflammatory reaction in the joints while a flexion contracture of the knee is being straightened out, and carrying it through until the patient can become ambulatory.

A somewhat more recent method of treatment is the use of hydrocortisone or compound F by injection directly into the joint. Because an effect is obtained in the treated joint only, its field of usefulness is necessarily restricted to those patients in whom one or two joints, frequently the knee, ankle or elbow, may be holding up the over-all treatment program. Table 7 summarizes our experience in the first 43 rheumatoid arthritic joints so treated. In 8 cases we did not get any particular response; in 5 we obtained an initial response which was not maintained with subsequent injections; in 30 a fairly satisfactory response was maintained with repeated injections. As to average duration of benefit, an occasional lucky patient has gone 4 to 6 weeks. The average dose injected at any one time was 25 to 37.5 mg. Much more experience will be needed before the proper place of this method of treatment in the long-range program of the management of rheumatoid arthritis can be defined.

MEETINGS AND POSTGRADUATE COURSES

American College of Chest Physicians: Sixth annual postgraduate courses on diseases of the chest, November 2-6, 1953, at the Hotel New Yorker, New York City. Tuition for the course is $75. Further information may be secured by writing to the Executive Director, American College of Chest Physicians, 112 East Chestnut Street, Chicago 11, Illinois.

Twentieth annual meeting, June 17-20, 1954, San Francisco, California. Physicians interested in presenting scientific papers on any phase in the diagnosis and treatment of heart and lung disease should send a 100 word abstract, not later than January 1, 1954, to Dr. Edgar Mayer, Chairman, Committee on Scientific Program, 850 Fifth Avenue, New York 21, New York.

The National Gastroenterological Association: Eighteenth annual convention and scientific sessions, October 12-14, at The Biltmore Hotel, Los Angeles, California. Program will include a symposium on cirrhosis of the liver, and panel discussions on peptic ulcer, diseases of the large bowel, and latest developments in cancer research. Following the convention, on October 15-17, the Association's fifth annual course in postgraduate gastroenterology will be given at The Biltmore Hotel and the College of Medical Evangelists, under the direction of Dr. Owen H. Wangensteen and Dr. I. Snapper. Further information may be obtained by writing to the Executive Officer, National Gastroenterological Association, 1819 Broadway, New York 23, New York.

University of Minnesota, Minneapolis: Continuation course on diseases of the chest, October 15-17, 1953. Visiting speakers will be Dr. Andrew Banyai, Associate Clinical Professor of Medicine, Marquette University Medical School, Milwaukee; Dr. Donald S. King, Consultant, Tuberculosis Service, Veterans Administration, Boston, and Dr. Dan Morse, Medical Director and Superintendent, Peoria Municipal Tuberculosis Sanitarium, Peoria, Illinois. Faculty will include members of the faculty of the University of Minnesota Medical School and the Mayo Foundation.

Digestive Diseases

WALTMAN WALTERS*

Mayo Clinic, Rochester, Minnesota

In the first of 2 cases a gastric ulcer was demonstrable by x-ray. In the second case it was decided that abdominal exploration was necessary to determine whether the obstruction was benign or malignant, although the latter seemed to be the case—probably a neoplasm of the pancreas.

I AM going to discuss with you 2 patients, both of whom I think you will find very interesting. When I wrote Dr. Stanley Hoerr that I would like to have patients with digestive diseases I did not ask for any specific ones. My reason for mentioning this is that you are seeing these patients about 15 minutes later than I first saw them, although I did have the opportunity of discussing them with Dr. McAfferty, who is a resident of the Cleveland Clinic, and with Dr. Skinner, who is an intern at the University Hospital.

WALTMAN WALTERS

Dr. McAfferty has had under observation this gentleman who was operated on by one of the surgeons at the Cleveland Clinic. Doctor, will you take two or three minutes to run over that history?

DR. MCAFFERTY: This 40 year old white male technician was first seen at the Cleveland Clinic in September 1952, complaining of epigastric distress for a period of one year, and in addition to that he had anorexia, weight loss of 35 pounds, and increasing constipation.

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

The pain was precipitated and aggravated by emotional stress and excitement and was not relieved by antacids or any particular foods. It was relieved somewhat by belching. The pain was epigastric and radiated through to his back.

He had been treated by his local physician, and an upper gastrointestinal series carried out in April 1952 was reported as negative.

When he was first seen at the Clinic his physical examination showed minimal findings, mainly evidence of chronic weight loss and some pallor of the conjunctiva and mucous membranes. There was no mass palpable in the abdomen. Liver, spleen and kidneys were nonpalpable; there was no particular tenderness in the abdomen.

Laboratory findings—Urine normal; hemoglobin 13 gm.; serum protein normal; BUN normal.

Gastric analysis showed 28 units free acid and total acid of 58. The secretion was positive for occult blood.

An upper gastrointestinal series in September suggested the presence of a small ulcer high on the lesser curvature. The Medical Department recommended a trial of medical treatment for one month. He was given ade-

quate therapy and was brought back for a repeat x-ray study and re-evaluation the following month, and at that time the ulcer was much larger than it had been when he was first seen. It was therefore advised that operative procedure be undertaken.

Five days ago (November 6) laparotomy was done. It was planned as a thoracoabdominal approach. The ulcer was found to be immediately adjacent to the esophagus, and it would have required a complete gastrectomy to remove it in a young man. We elected to do a 50 per cent resection, which we have done, and at that time the stomach was opened and four biopsies were taken from the ulcer site, deep in the crater and deep in the margin. Frozen sections showed all biopsies were benign, so the stomach was anastomosed to the intestine by the Hofmeister technic. He has made a good recovery. He has had none of his preoperative ulcer pain and has been ambulatory since the day of surgery.

DR. WALTERS: Thank you very much, Dr. McAfferty.

I think you will all agree with me that this has been a triumph of surgical treatment of a chronic, progressive gastric ulcer. I hope you took cognizance of the gastric acidity which Dr. McAfferty reported and which Dr. Lahey* referred to also in his cases; that is, sometimes knowledge of it is helpful and sometimes it isn't. The presence of hydrochloric acid in a patient with an ulcerating gastric lesion, even though it looks to the roentgenologist as though it were benign, does not exclude malignant change being present in the ulcer.

The operation which was performed was of the Hofmeister type which Dr. Lahey also showed you. In this way you can narrow the lesser curvature down to get a stoma of as small a size as you wish; or you can, as some others do, make a valve which is thought to be a true valve, and then bring the jejunum up to it. The two are a little different, but the trouble with the valve is that it does not last very long. It flattens out, and then you really have the smaller stoma. Unfortunately I have seen a few cases where the stoma has been made so small that the patient has had the same vagotonic symptoms as though the distention occurred in the jejunum; that is, the distention occurs in the stomach but produces the same vagotonic symptoms. So one can get the stoma too small.

A few years ago, roentgenographically, I studied the postoperative effects of the Polya, and contrasted them with results in a group in which we narrowed the lesser curvature or made a valve. Sir Henry Ogilvie has expressed the belief that the valve prevents regurgitation into the proximal loop. Our studies showed that only a few patients had regurgitation of barium into the proximal loop, regardless of whether the Polya or the Hofmeister modification had been performed, and whether they did or whether they did not was not an indication of whether they would have vagotonic symptoms.

I think some of the best studies on the vagotonic symptoms after resection have been done by Machella at the University Hospital in Philadelphia. In his experience and in ours at Rochester, it makes little difference whether you anastomose the entire circumference of the stomach and the jejunum (Polya) or whether you use a Hofmeister technic and narrow the circumference. Other factors also are concerned which we have not time to discuss now.

If anyone had told me 32 years ago that 32 years later I would see a man who only five days ago had a high gastric resection for a high gastric ulcer, presented at the Interstate Postgraduate Medical Assembly with his clothes on and looking as though he were getting ready to go out and see the Cleveland Browns play, I wouldn't have believed it. This seems to me to be a very fine example of the improvement which has occurred in surgery and its related fields—anesthesiology and so on. This case demonstrates also the benefit derived from the use of substances such as blood and electrolytes prior to operation.

As far as the operation is concerned, I believe this is a better type than total gastrectomy would be in these circumstances, because I think one should save for the patient

*Lahey, Frank H.: Recent developments in the management of peptic ulcer. Postgrad. Med. (To be published.)

TABLE 1

SERIES 3L

PERCENTAGE OF PATIENTS REPORTING SATISFACTION, GIVING EVIDENCE OF FREEDOM FROM ULCER SYMPTOMS AND SHOWING EVIDENCE OF SATISFACTION

SITE OF LESION, HEMORRHAGE, APPROACH AND OPERATION	PER CENT OF PATIENTS			
	Satisfied	*Not satisfied*	*Free of ulcer symptoms*	*Evidence of satisfaction**
G.J.U.				
Without hemorrhage				
Thoracic; alone	82	13	80	76
Abdominal; alone	77	17	83	73
With hemorrhage				
Thoracic; alone	80	10	80	73
Abdominal; alone	89	7	87	84
G.U.				
Abdominal; with G.R.	76	4	76	63

*Reports and evidence of satisfaction; relief of pain; freedom from ulcer symptoms and ability to work.

Explanation: 3L is a series of cases reported from the Vagotomy Committee study, consisting of reports from surgeons who had performed more than 50 vagotomies. This table is an extract from Table 5 of "Comparison of results in personally studied cases in which gastric vagotomy was performed with those reported to the American Gastroenterological Association." Gastroenterology 19:623-638 (December) 1951, by Waltman Walters, M.D., Hiram H. Belding, III, M.D. and M. Katharine Smith, B.A.

as much of the stomach as possible and still accomplish the physiologic result which one hopes to obtain, together with relief of the patient from his pain and indigestion. The surgeon can attain these objects and return the patient to his work with little possibility of recurrence by doing a Hofmeister resection, including the ulcer in the segment of lesser curvature removed. I might say that I never have seen a gastric ulcer recur after proper resection has been done. I do not like to leave a gastric ulcer, even though it has been biopsied and the examined specimens have been reported as benign. And let me say right here and now that anything I may say in the discussion of these 2 cases is in the interest of our patients and ourselves and is to be considered as discussion and not as unfavorable criticism. I think that on occasions one can be content with the procedure which was done in this case, and I would have no hesitation in doing it at any time. On the other hand, I feel that if one uses this Hofmeister principle, one can remove the upper third of the lesser curvature of the stomach, joining the remainder either to the duodenum as a Billroth I or to the jejunum as a Polya, thus removing the ulcer and accomplishing the same results as though one didn't have to make such a high resection. It is possible nowadays, with the complete relaxation obtainable through various types of anesthetic measures, to get right up to the lower 5 cm. of esophagus and to remove lesions at the cardiac end of the stomach.

As I say, I am prejudiced against total gastrectomy in the treatment of benign gastric ulcer, for the reason that I think it is too radical a procedure for the type of lesion which is present, particularly when one can obtain equally good and probably better results if one does subtotal gastrectomy.

I am not in accord with vagotomy and leaving the gastric ulcer. I did this in 5 cases of gastric ulcer and reported 2 recurrences. Apropos of that are the statistical data to which Dr. Lahey referred (Table 1). The bottom column, you note, lists gastric ulcers. These are the numbers reported by the Vagotomy Committee, assembled from reports of more than 100 American surgeons. A very small number of patients with gastric ulcer had vagotomy.

These patients are a very select group, and

you will notice that all of them had gastric resections in addition to the vagotomy. Vagotomy was done on the man just presented in order to mobilize the esophagus, which they were able to do. Dr. McAfferty, however, did not say whether the surgeon who operated felt that it was an addition to the surgical procedure. Personally I don't think it is. In the average type of patient, instead of obtaining, say, a 95 per cent or better excellent result which one should expect as a minimum in resections for chronic gastric ulcer, you see that only 76 per cent were free of ulcer symptoms and satisfied with the operation. This is the result of resection and vagotomy as reported by American surgeons.

There is a much higher incidence of fine results following resection alone; in fact, I think the results of resection of the stomach for chronic gastric ulcer are some of the best in surgery—better than 95 per cent excellent.

Dr. Skinner, can you tell us about this lady's case just as you and I discussed it?

DR. SKINNER: This 52 year old woman four months ago woke up in the middle of the night with an acute attack of right upper quadrant pain radiating around to the back, which lasted three to four hours. Since then she has had these attacks off and on to the present, and in between a dull pain in the right upper quadrant. Two months ago she began to be anorexic and had attacks of nausea and vomiting. The vomitus usually was clear and at times had a brownish material in it. She had chills and fever.

One month ago after a particularly bad night with this pain in the right upper quadrant she noted that her sclerae were icteric, and following that her skin became progressively more yellow, her stools lighter colored—as she described it, "light and soapy"—and her urine darker.

She was seen one week ago and was admitted to University Hospital. On that admission her urine was normal except for the positive bile, her white count was normal and her bilirubin was elevated (direct, 7.4; total, 10.4); a few days later the bilirubin was up to 13.2.

Her alkaline phosphatase was 12.7; amylase was normal; prothrombin was slightly low but came back with vitamin K to 80; total proteins were normal.

DR. WALTERS: Will you speak a bit about the x-ray examination, Dr. Skinner?

DR. SKINNER: At the age of 18 she had an empyema on the left, and the ninth rib was resected, so we took some x-rays. That seems to have been resolved all right, but there is some basilar atelectasis on both sides. Because of the brown color in the gastric vomitus, an upper gastrointestinal series was done and it was read as hypertrophic gastritis.

DR. WALTERS: Before we examine this patient I would like to go over just a few of the details of this history as I remember them.

Four months ago this lady began having attacks of biliary colic—typical attacks, no jaundice, however, no evidences of obstruction of biliary type—and she was an outpatient then in a clinic in another city. Then she came here about eight weeks ago and had these attacks and was seen as an outpatient. Then about four weeks ago she became jaundiced but she did not become jaundiced particularly after a colic; that is, she wakened and found she was jaundiced. Is that correct? You correct us, Mrs. K., if there is anything with which you don't agree.

Do you have any abdominal pain now?

PATIENT: Yes.

DR. WALTERS: Where is it?

PATIENT: Right here, radiating to the back.

DR. WALTERS: Is it better or worse when you are sitting up?

PATIENT: Just about the same, a little less.

DR. WALTERS: When you lie down flat you have more pain, and where?

PATIENT: Right here.

DR. WALTERS: And in the back?

PATIENT: The same.

DR. WALTERS: These are all doctors and they appreciate your coming here. I hope you don't mind my just examining your abdomen. I examined her abdomen a few moments ago. Would you think there is a little fluid in there, Dr. Skinner?

DR. SKINNER: Yes.

DR. WALTERS: Did you feel a gallbladder that was distended?

DR. SKINNER: I didn't.

DR. WALTERS: Neither Dr. Skinner nor I could feel a distended gallbladder.

What is the nature of her stools?

DR. SKINNER: They are very light colored.

DR. WALTERS: A few minutes ago I went in to see her and she was sitting up. She thought she was vomiting a little fluid. I thought, "Well, she has a little gastric retention with a little overflow, and that looks to me like bile." Dr. Pfeiffenberger, take a look at this for me. What color does that look like?

THE SPEAKER: Well, it has three colors; it is dark brown like coffee, and then it looks like the skin of some sort of fruit in it, and then there is a green color.

DR. WALTERS: It looks a little like bile.

THE SPEAKER: Yes, sir.

DR. WALTERS: I knew if we kept him up here we would get the right answer. I said to myself, "Well, I am going to make quite a diagnosis on this case because there is bile in the stomach." But it isn't bile. The yellow in what she vomited isn't from her stomach; it is the yellow from the tissue she had used to wipe her mouth. We had her discard that, and examined another specimen. It was frothy, like what comes from the lungs, not what you usually see from the stomach. Then Dr. Skinner tells me that the gastric analysis has been made and there has been no bile in the duodenal content.

Here is our president, Dr. Sturgis, one of the finest internists in our country. I am sure he has been listening to this, and we would like him to come up and participate in this discussion if he will. Dr. Sturgis, what else would you want to know about this patient to make a diagnosis? Four months ago and for three and a half months biliary colic, then jaundice without pain, distended abdomen containing fluid, clay-colored stools, no bile in the duodenal content, liver function test excluding an intrahepatic cause for her jaundice, and here she is.

DR. CYRUS C. STURGIS: I think she has a neoplasm, and the reason I think so is because she has ascites, but I do not see what you can do, very much further, without an exploratory laparotomy to be certain. The older I get the more I am in favor of exploratory laparotomies, after you have exhausted all other possibilities, to try to settle the diagnosis once and for all.

DR. WALTERS: You stay here and let's do this together.

DR. STURGIS: This is *really* extemporaneous.

DR. WALTERS: Come on, Dr. Lahey; we want to have you in on this, too. I don't know whether Dr. Lahey has been listening or not.

DR. FRANK H. LAHEY: Yes, I have.

DR. WALTERS: We have had a fine association as golf companions and speakers at surgical meetings over about a 25 to 30 year period during which I have learned a tremendous lot from Dr. Lahey. Sometimes we have disagreed in the meetings but never on the golf course. At any rate, Dr. Lahey, what do you think about this lady?

DR. LAHEY (palpating patient's abdomen): I would agree with everything my medical-surgical friend from Ann Arbor has said. He is the most surgical medical man I have seen for a long time.

DR. STURGIS: I have learned by experience, Dr. Lahey.

DR. LAHEY: I wish more medical men would be that surgical and come more and more to exploratory laparotomies when everything else has been exhausted. I am sure he is not in favor of what we surgeons used to be when people said of us that we never used our heads to make a diagnosis, we only used our hands, but after everything has been exhausted, as he has said, I agree.

I don't know about the fluid. If she has fluid that is certainly additional evidence.

DR. WALTERS: I am particularly happy to have Dr. Sturgis and Dr. Lahey discuss this case because I think this is the type of case in which cooperation and collaboration in the study of the patient will improve the result of the treatment which is instituted. I have been mistaken so many times on operating on patients with various degrees of biliary obstruction, thinking that one type of lesion was present and finding another at operation, that I have come—and did come a long time ago—to the decision that wherever there is a question in any case, not just in cases of

TABLE 2

BASIC LABORATORY DATA IN VARIOUS TYPES OF JAUNDICE

CONSTITUENTS OR FACTOR	IN JAUNDICE CAUSED BY		
	Hepatitis	*Stone*	*Carcinoma, ducts or pancreas*
Blood lipids	Normal or diminished	+	++
Alkaline phosphatase	Normal or diminished	+	+
Serum globulin	++	Normal	Normal
Bile in duodenal drainage	+	±	−
Prothrombin response to vitamin K	None	+	+

+=positive.

++=strongly positive.

±=positive or negative.

biliary obstruction, abdominal exploration should be done. Now, with the risk of exploration so low, we must remember that even with the excellence of our diagnostic methods there will be some obscure cases in which it is impossible to make a differential diagnosis, and in fairness to the patient we must use that additional diagnostic method, which also can be used as a method of therapy, namely, abdominal exploration.

Apropos of that, let me just speak of a patient I operated on a few days ago. This woman had had two previous operations on her biliary tract by a friend of mine, an excellent surgeon. At the last operation he thought that she had intrahepatic jaundice and he did not explore the common duct. It had been explored at the previous operation. There was clear bile in small quantities in the duodenal contents and there was some change in the new and fairly accurate tests of liver function. Results of these tests, by the way, are never to be accepted beyond the fact that they are results of tests, and they never are to be allowed to overrule one's clinical judgment. Well, I was ready to turn this patient down, thinking that it had been proved that the obstruction was intrahepatic, but a young medical man who had been seeing this patient every day and studying her symptoms said, "I think she should have exploration." I talked to the family and said, "I don't think there is 1 chance in 10 that there is an organic lesion of the biliary tract. On the other hand, the lady is having these attacks of severe pain; medical treatment has failed to prevent it and there is no way to determine for sure that a removable cause for her pain doesn't exist without an operation; so I think we should operate on her."

She had an incomplete stricture of the common duct and we were able to do hepaticoduodenostomy.

Another day I saw a woman whose initial symptoms, as recorded by the internist, were nervousness and unhappiness. She had undergone cholecystectomy two years before. The gallbladder didn't contain stones. She had continued to have attacks of pain. She had had no evidence of biliary obstruction. It seemed to the medical man that she might have something in her common duct. I thought maybe it was one of those spasms of the sphincter and I told her, "I don't know what we are going to gain out of this operation and we may not gain much if there is not a pathologic lesion."

But I did an exploration and she had an elongated stump of cystic duct with two small gallstones in it, with one of the stones obstructing the cystic duct, and there was clear fluid in back of it.

I would like to say that I think in the handling of the case of Mrs. K., whom we presented, a little gas or a little local anesthetic, or whatever other light anesthetic you please, and an exploratory incision will be more helpful than any other test that might be done.

The data in Table 2 are helpful in determining the degrees of liver disturbance in relation to what seems to be obstructive extrahepatic jaundice. To learn how much disturbance there is in the liver, I rely on three tests. What is the prothrombin time? Is it elevated? If so, there is disturbance of liver function, especially if it doesn't respond to vitamin K. Dr. Skinner in his data here showed that it was a little elevated. What has been the course of the serum bilirubin? Has it increased? Has it decreased? Has bile been obtained in the duodenal contents? If there is no bile in the duodenal contents, if the serum bilirubin or jaundice is increasing and if there are clay-colored stools, it is almost certain to be a neoplasm in the head of the pancreas, or at the lower end of the common bile duct, or in the common bile duct, or starting in the gallbladder and obstructing the common bile duct. Those are important criteria. If there is prompt response to vitamin K of an elevated prothrombin time, you know there isn't a great deal of damage to the liver.

I am not going over these tests other than to call your attention to the fact that there was no bile in the duodenal contents in this woman's case, or in her stool. You will notice she did not have an elevation of her alkaline phosphatase or of her serum globulin. On the other hand, in hepatitis there is an increase in the serum albumin. What is an easy way to remember that? Well, you get a reversal of the A-G ratio. When there is a reversal of the A-G ratio, then look out for more trouble in the liver of the patient with obstructive jaundice than you think exists.

I find it difficult to correlate these findings in a practical fashion with what we have tried to do here this morning in determination of the type of lesion this woman has. I think you will find the cephalin-cholesterol flocculation a little difficult to interpret, except for the fact that with high values, when there is bile in the duodenal contents, the condition is more apt to be intrahepatic, infectious hepatitis than jaundice, which is not due to trouble in the liver.

Dr. Sturgis, do you want to comment?

DR. STURGIS: No, except I certainly agree with you. The absence of bile, of bilirubin from the duodenal contents, to me is a very convincing fact that there must be obstruction probably due to malignancy rather than to stone. In stone, it rarely entirely excludes bile from the duodenal contents. Then, of course, there is the presence of ascites. Intrahepatic jaundice has come in the last few years to add some confusion to this whole picture, but I agree with what you have said. However, here I do not see that you can do anything further except to settle it, as you say, by an exploratory laparotomy.

DR. WALTERS: Dr. Lahey?

DR. LAHEY: I think I can feel this woman's gallbladder. I think she has a positive Courvoisier sign; she has jaundice and distended gallbladder, but it would be easy to settle and it should be easy to determine whether or not exploration ought to be done. If she has distended gallbladder with jaundice and with pain and she has lost 41 pounds in weight, the only thing I believe you could do would be to make her more comfortable by doing a palliative operation, but I would like to have her have a flat plate and know whether or not she has a distended gallbladder, because that would certainly make positive the diagnosis of carcinoma of the head of the pancreas.

You really ought to get the three of us up here together oftener.

DR. WALTERS: Thank you, Dr. Sturgis and Dr. Lahey.

Surgical Treatment of Ulcerative Colitis

RICHARD B. CATTELL*

Lahey Clinic, Boston

The surgical treatment of ulcerative colitis has greatly improved in recent years, reflected best by the reduction of operative mortality from 20 per cent to 5 per cent. Indications for surgical intervention are discussed. Experiences with approximately 400 patients treated surgically at the Lahey Clinic are reported, including an improvement in the management of ileostomy.

RICHARD B. CATTELL

My subject is one that is concerned with many tragedies—tragedies resulting from delay before adequate treatment is given, tragedies because medical treatment may be ineffectual and too great a delay occurs before operation when a surgical indication has developed, and tragedies, too, because in the past when surgical treatment was instituted, even successfully, the patient was left in a state that is not consistent with normal or happy activity.

Fortunately that has changed, and to demonstrate this change I would first like to present the results of surgical treatment in an earlier period.

During a period of 20 years at the Lahey Clinic we have operated on approximately 400 patients in the acute or chronic stage of ulcerative colitis. In the early part of this period, too often we were not successful in obtaining a satisfactory result and the operative mortality rate was high. For the first 103 cases in a 10 year period there was a patient mortality rate of 20 per cent, or an operative mortality rate for individual operations of 9.3 per cent. Similarly, during this period the immediate postoperative care of the patient with an ileostomy was very trying, not only from the patient's and the surgeon's point of view but particularly for the nurses responsible for the immediate care of these patients in the hospital. Fortunately, with the second larger group of 300 patients during the past 10 years, I can report a much more satisfactory treatment and, as I will outline later, a very low operative mortality rate.

Through the courtesy of Dr. Rupert Turnbull here in Cleveland, we are presenting a 25 year old farmer who had had severe diarrhea since 1945. There were intervals when he was symptom-free and felt quite well, but during attacks he had 25 to 30 bowel movements a day, occurring with equal frequency at night so that his sleep was disturbed, and he gradually lost weight until he was down to 120 pounds from a normal of approximately 160 pounds. The bowel movements consisted not of fecal material but chiefly of mucus, pus and blood; constant tenesmus followed a sat-

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

isfactory evacuation and continued until a new evacuation was attempted.

This man represents very well the failure of medical treatment. Many such treatments have been described, each offering considerable promise and most of them offering improvement, but few offering real cure or permanent relief. They have been responsible for amelioration of symptoms rather than for cure of the underlying disease.

This patient had a long trial of medical management, beginning about four years ago. I would like to call your attention to the fact that the diagnosis was not made until a year after the onset of the disease. During that year he was given various agents and drugs for relief of diarrhea, but the diagnosis of ulcerative colitis was not established. This can be done by only two means: (1) sigmoidoscopic examination and (2) barium visualization of the colon.

Following this he had the usual medical supportive treatment, including the sulfonamide drugs that have been reported so favorably; AUREOMYCIN®, and a course of vaccine therapy. His symptoms were ameliorated for one period of 18 months.

This man is quite disturbed and frightened at coming out here, although I assured him you were sympathetic with his problem and that he can help us in a consideration of this disease, which he is quite anxious to do. He is not a nervous person and was not nervous before ulcerative colitis developed. Dr. Turnbull mentioned a little earlier that this perhaps does not represent the typical patient with ulcerative colitis, who is an asthenic, nervous individual with problems that could be considered psychosomatic in nature. I believe from my experience that this is overemphasized; it is not that psychiatric treatment may not be beneficial while the patients have the disease and in the period of rehabilitation following adequate therapy, either medical or surgical, but if you are so unfortunate, as this patient, in having 25 or 30 bowel movements a day you would, I am sure, become quite nervous. I think the nervous symptoms are much more likely to follow the disease itself. Even when nervous symptoms are particularly prominent, many of these patients appear quietly confident and composed after relief of their disease.

This patient found that he could not work, and for two months last summer he refrained from all types of productive activity. He came to his physician in the hope that something other than medical treatment could be done. A roentgenogram of the colon taken at that time shows the feathering of the mucosa that is typical of chronic ulcerative colitis after evacuation of barium. In areas the film suggests pseudopolypoid formation that occurs not because of hypertrophy of the mucosa so much as because islands of mucosa are left between the large ulcerations. There is no particular irregularity to suggest malignant degeneration.

We have just begun to note the depression of the hepatic and splenic flexures of the colon. Usually after a period of five years we see a greater degree of contraction of the colon than is obvious in this case.

The patient underwent operation on August 19, 1952, with removal of the colon and formation of an ileostomy. I have asked him to demonstrate an apparatus which he is now wearing, one that is used in our clinic during the immediate postoperative period, with many patients continuing to use it permanently. This is the Torbot bag, a plastic ring with a detachable rubber bag. The rubber bag can be changed at any time. The plastic ring is cemented to the skin, and only a few moments are required to remove and reattach it.

He was a little hesitant about showing the lower end of this bag because it has a paper clip on it. Anything that closes it off is quite satisfactory, and you will find that all these patients will modify their bags to suit their individual problems.

During the three months since operation, this man has had a complete rehabilitation and has gained 47½ pounds. That perhaps is the best reflection of the change in his health, and this gain began almost immediately following operation and has continued steadily. He now weighs 170 pounds, more than he weighed before he became ill. (To the patient): When do you change this bag?

PATIENT: The first thing every morning.

DR. CATTELL: How do you attach it to your skin?

PATIENT: I glue it to the "stomach," put glue on the plastic ring and also on the "stomach," let it dry completely, and it sticks for approximately 24 hours.

DR. CATTELL: How often does this bag become loose?

PATIENT: It begins to loosen in about 24 hours. It will stay on that length of time, but it is easy to take off.

DR. CATTELL: Do you take a shower or a tub bath?

PATIENT: I can take either.

DR. CATTELL: Does it cause any loosening of the bag?

PATIENT: No, not a bit.

DR. CATTELL: What have you been able to do since you returned to work after recovery from the operation?

PATIENT: I do all my work. I have been picking corn. I have 30 acres and I am also picking some for my neighbors; it totals 62 acres altogether.

DR. CATTELL: It seems to me that when I said his weight gain was the best indication of his rehabilitation I overlooked something. His ability to pick 62 acres of corn perhaps gives you a little better idea of what has been accomplished.

One of the important points that has been raised relative to abdominoperineal resection for ulcerative colitis and also for rectal carcinoma has been a disturbance of sexual relations following such a procedure. This man tells me that he has had no disturbance of libido, potency or ejaculation—the three things that may be modified following total colectomy. He has been married for several years and is the father of a 4 year old child.

If a patient has an ileostomy, how much does it shorten his life? If no obstruction or other complication associated with the operative procedure develops, there is no shortening of the patient's life. The longest that I have followed a patient with ileostomy has been 23 years. This patient is perfectly well and has carried on normal activity during this entire period since ileostomy and total colectomy.

Is their nutrition reasonably good without the absorptive function of the colon? I can assure you that there is no difficulty in this respect; in fact, most of these patients tend to become obese.

The three operative procedures that are effective in ulcerative colitis are ileostomy, partial or segmental colectomy and total colectomy. A few patients can be successfully treated by means of partial or segmental colectomy, but ileostomy and total colectomy will be necessary in most of the patients submitted to surgery.

It is quite important, when ileostomy is done, that the ileum be brought out to at least an inch or an inch and a half beyond the level of the skin. In addition, it must be brought out in a straight direction so that it is not curved over, which results in an ileal discharge directed toward the skin.

The decision to do a skin graft, as Dragstedt has recommended, depends on the surgeon's preference. We caution against this. All that is necessary is to wait a short period of time for the mucosa of the ileal lining to grow down to the skin, and from that time the ileostomy should function well.

At the time of ileostomy, immediate decompression must be carried out by means of a catheter. The decompression catheter is left in for four days, following which a temporary type of apparatus such as the Perry bag is fitted. Many types of apparatus are available, and most of the manufacturers are persons who have had ileostomy. The Perry bag is attached to the skin and over the stitches by means of double-coated SCOTCH® tape. It can be fitted to any ileostomy immediately and there should be no ileal discharge on the skin.

About the seventh to the tenth day, if use of the Perry bag is not continued, we use the Torbot bag such as the man I presented earlier was wearing; this type is utilized for three months. Subsequent to that, a different type of bag can be used—the Rutzen-Koenig bag, which is made in Chicago, or the Permatype bag, which is made in Hartford, Connecticut. The latter can be worn for much longer periods of time. A Permatype bag put on with the type of cement available today can be

worn two or three weeks without changing.

There is little odor connected with these bags, particularly if they are changed every 24 hours and a second bag is used for the next 24 hours. That is perhaps the most satisfactory way of avoiding odor.

This man dilates his ileostomy by means of a 12 mm. bougie. The simplest method of keeping it open (and it tends to contract at the level of the skin) is merely to teach the patient before he leaves the hospital to insert his finger past the second phalangeal joint into the ileostomy and dilate it gently before the bag is reapplied. In doing this he will make certain that he does not have narrowing and the complications associated with it.

A number of things can happen to an ileostomy. If the bag is improperly fitted it may irritate the side wall of the ileum and produce a fistula. If the opening in the abdominal wall is allowed to contract, a spontaneous fistula may develop. In this case a serious situation is likely to arise in that skin irritation will develop, the bag cannot be fitted properly, and there may be a disturbance in the fluid and electrolyte balance. If a fistula is encountered, further surgical intervention should not be delayed. The ileostomy should be detached from the abdominal wall, the area of fistulous involvement excised and a new ileostomy made.

In the case described, the patient presented himself for surgery when he was in a chronic state. In spite of his considerable weight loss and general poor nutrition, he still, in his youth of 25 years, could be submitted to this operation in one stage; in other words, he had an ileostomy and total colectomy as a one stage procedure. I would like to caution against doing this many times. We have done it a few times. Dr. Ravitch in Baltimore reported 12 or 13 cases a few years ago and we realize that it can be done from a technical point of view. However, particularly in the patient who is acutely ill and "toxic" from the infectious process, no more than an ileostomy should be done at the first stage, the colectomy being delayed until a later date.

The interval between the operative stages should be long enough to permit the patient to gain as much as possible from the previous procedure. This may require three to six months. Many patients with ulcerative colitis are young, still in the high school, college or university age levels, and if an ileostomy is utilized to get them over the acute emergency the colectomy can be delayed until the following summer. This will permit the patient to engage in his educational activities during that time, and the abdominoperineal resection can be completed subsequently.

Among the indications for surgery is acute fulminating ulcerative colitis. If improvement does not occur after five to seven days of medical management, ileostomy should be performed. This reasonable delay is justifiable, since some patients will respond satisfactorily on medical management. In our clinic we believe that if ileostomy is employed early in the acute fulminating group the mortality rate will be lower than if there is delay in accepting ileostomy.

The second indication for operation is hemorrhage. Only 5 per cent of patients with ulcerative colitis have hemorrhage which could be termed massive. Chronic loss of blood is, of course, a conspicuous feature in most cases.

When free perforation of the ulcerated colon occurs, death is very likely to result, but subacute perforations resulting in fistulas between the various abdominal organs and abdominal wall, vagina and bladder are common, and once they have occurred, only operation will relieve that patient.

A small group of patients may require operation because of persisting infectious arthritis. In our experience, if this is neglected and these patients are allowed to go on year after year, they will have such marked deformity of their joints that they may become incapacitated.

In some patients obstruction is the operative indication. This, of course, is a late cicatricial complication of the disease in which healing of the ulcerations results in a greatly diminished lumen of the bowel.

The next indication is that of malignant degeneration. Bargen and his associates recently reported on 73 adenocarcinomas of

the colon found in patients with chronic ulcerative colitis. In that entire group, 40 were submitted to resection, and of the 73 patients only 2 survived for five years. We have had 22 patients who had malignant degeneration in ulcerative colitis. Only 2 in this small group have survived five years, and in both the lesion was discovered coincidentally when total colectomy was done for some other indication.

The final indication for surgical treatment in ulcerative colitis is intractability. These are patients whose symptoms persist in spite of adequate medical treatment, and who are unable to work.

Relative to what has been accomplished since the initial 10 year period referred to earlier in this discussion, I want to call your attention to the reduction in the operative mortality rate. Of 141 patients operated on in a three and a half year period, 6 died, a mortality rate of 4.3 per cent; of 104 patients who had total colectomy, only 1 died. Two patients died after ileostomy.

I cautioned you a little earlier about employment of total colectomy or subtotal colectomy at the time of ileostomy, and the reason for this is supported by our experience. Three of the 6 deaths in 141 cases were of patients whose disease was in the chronic stage, in whom ileostomy and colectomy were done at the same time. We have been doing this now since 1935 in a selected group of patients, but they must be carefully selected and only the best risks should have subtotal colectomy done along with the ileostomy.

With rare exceptions patients who have had ileostomy will subsequently require colectomy. We often hear the remark that the colon should be left even though ileostomy is required because if we discover the cause of the disease or a new method of therapy, of which we have had a succession that have unfortunately failed, it might be possible to permit these patients again to utilize their colons. This is fallacious reasoning, because the structural change in the colon is so great that even with cure of the disease the colon would be incapable of satisfactory function.

Finally, on the basis of this experience in the treatment of a large number of patients with chronic ulcerative colitis, we would like to sound a hopeful note relative to surgical treatment. We do not wish to apply surgical treatment in those cases that can be handled successfully medically, but when medical treatment fails or there are complications, we can now assure the patient that operation can be done with relative safety, and it can eradicate the disease.

Postgraduate Clinical NOTES

14. MEDICAL APPROACH TO DISABILITY EVALUATION

The approach to the examination of a claimant for disability involves many factors that would not be considered in the regular doctor-patient relationship. The examination will include (1) history, (2) clinical findings, (3) laboratory and x-ray findings, (4) opinion and state of disability—*a*, total disability (as to temporary total; permanent total); *b*, partial disability (as to temporary partial; permanent partial).

Earl D. McBride, *Industrial Medicine and Surgery*, November 1952, p. 519

Medical and Surgical Management of the Patient with Mitral Stenosis

F. MASON SONES, JR.* AND DONALD B. EFFLER**

Cleveland Clinic, Cleveland, Ohio

The value of mitral commissurotomy in the treatment of mitral stenosis has been well established. Present concepts of the indications for and contraindications to operation, operative technic, pre- and postoperative management, and results of treatment are briefly discussed in a combined medical and surgical clinic.

F. MASON SONES

DONALD B. EFFLER

DR. SONES: If five years ago one of us had proposed to open a chamber of a seriously damaged human heart and to work there for 10 to 15 minutes, he would have been considered a candidate for psychotherapy or the homicide squad. The experience of the last four years has changed all this, and it is now possible to state that in carefully selected cases mitral commissurotomy offers the most effective available treatment for mitral stenosis due to rheumatic fever.

The hazard of operation is minimal. In a small but representative series of 32 patients there have been 2 operative fatalities. One additional patient died three months after operation. Benefits were obtained in over 90 per cent of the surviving patients.

Selection of Patients for Commissurotomy

As physicians it is our desire to select those patients with mitral stenosis who will benefit most from commissurotomy. With this in mind, patients with mitral stenosis may be classified into four groups which are based on the amount of disability present as the result of a fixed obstruction to blood flow across the mitral valve orifice (Table 1).

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

Patients in group 1 are asymptomatic. They have to be told they have heart disease, and this is recognized usually during the course of routine physical examination. They present only auscultatory findings of mitral stenosis, and have a normal heart size and electrocardiogram.

Group 2 consists of patients who have symptoms due to mitral stenosis but have not reached the phase of congestive heart failure. We have divided these into two subgroups. The first is the phase of left auricular stress. These persons usually are comfortable at sedentary levels, but with unusual physical or emotional stress they experience severe dyspnea. Nocturnal dyspnea and even acute

pulmonary edema are not uncommon in this group. The trademark of this subgroup is isolated left auricular enlargement, often in the presence of a heart of normal over-all size. The electrocardiogram frequently shows broadened P waves in standard leads, and diphasic P waves in leads from the right precordium characteristic of left auricular enlargement.

Patients with significant pulmonary hypertension actually are suffering from another disease superimposed on mitral stenosis. They have obstruction to blood flow at the mitral valve orifice, but in addition there is increased resistance to blood flow through the pulmonary arterial bed, adding to the pulmonary hypertension and the burden on the right ventricle. Left auricular and right ventricular enlargement are demonstrable roentgenographically and fluoroscopically. Electrocardiograms reveal evidence of right ventricular hypertrophy or incomplete right bundle branch block.

Patients in group 3 have reached the stage of congestive heart failure, but the condition is amenable to medical control.

Irreversible congestive failure characterizes the cases in group 4. The myocardium has been irreversibly damaged and all measures of medical therapy fail to bring even temporary relief.

At present we feel that the ideal candidate for mitral commissurotomy falls in group 2 or 3. Patients in group 1 are not considered for operation because there is as yet no information that leads us to believe that the prognosis is any better with than without operation. Group 4 patients usually are not considered because previous experience indicates that mitral commissurotomy will not improve the irreversible myocardial damage that has occurred. Therefore, the symptomatic patient in group 2 and the patient in group 3 are candidates for operation except in the presence of the following contraindications:

1. Active rheumatic carditis—two years.
2. Bacterial endocarditis.
3. Intractable myocardial insufficiency.
4. Coronary insufficiency.
5. Recent embolization.
6. Age below 18 years.

TABLE 1

CLASSIFICATION OF PATIENTS WITH MITRAL STENOSIS*

1. Asymptomatic
   - Auscultatory findings only
   - No disability
   - Normal heart size and electrocardiogram
2. Symptomatic (never in congestive failure)
   a. Left auricular stress
      - Paroxysmal dyspnea
      - Left auricle enlarged
      - P wave changes in electrocardiogram
   b. Pulmonary hypertension
      - Fatigue
      - Hemoptysis
      - Left auricle enlargement
      - Right ventricle enlargement
      - Right ventricular hypertrophy
      - Right bundle branch block
3. Congestive heart failure
   - Amenable to medical control
4. Irreversible congestive failure

*Based on amount of disability present as the result of fixed obstruction to blood flow across the mitral valve orifice.

7. Primary mitral insufficiency or aortic valve lesion.
8. Renal failure.

Active rheumatic carditis is an absolute contraindication to operation. Our concern is with the presence of active inflammatory changes in the valve itself. If fracture or incision is made in such a valve, it is anticipated that further deformity or reapposition of valve cusps will occur.

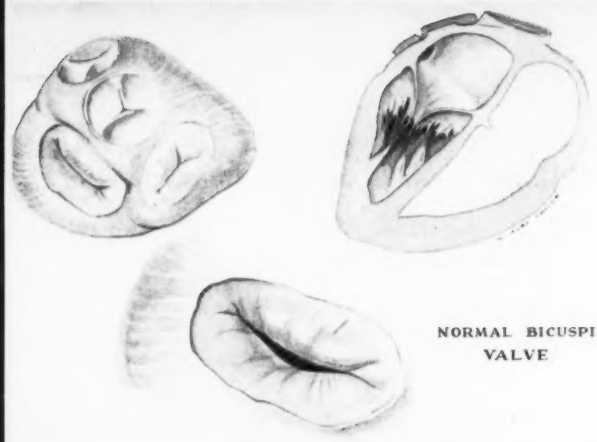
We think it is preferable not to operate in the face of a recent systemic or pulmonary embolism. We prefer to control these complications prior to surgery.

At present it is thought that persons younger than 18 years of age should not be considered candidates for operation because of the great possibility of recurrence of active rheumatic carditis. The upper age limit has not been established.

Renal failure or any other disease limiting a reasonable estimate of life expectancy to less than five years probably constitutes a contraindication to surgical intervention.

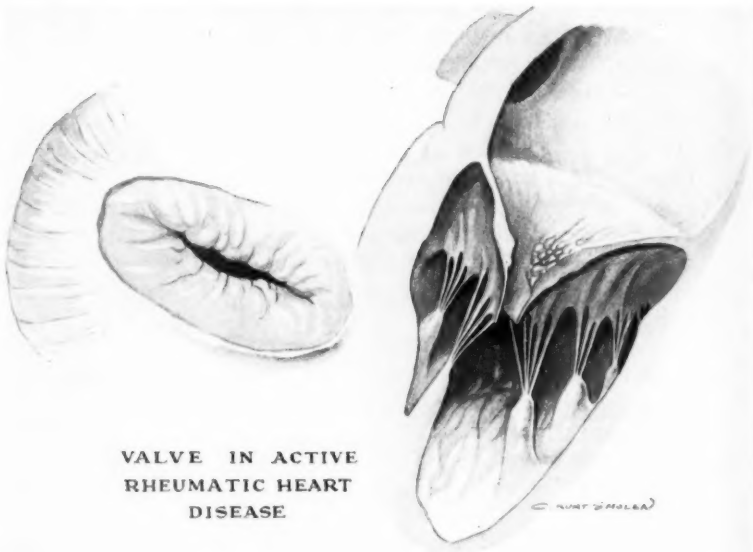
Preoperative Preparation

Commissurotomy should never be regarded



NORMAL BICUSPID VALVE

FIGURE 1 *(above)*. Normal mitral valve.



VALVE IN ACTIVE RHEUMATIC HEART DISEASE

FIGURE 2 *(right)*. Mitral valve in active rheumatic heart disease, illustrating the large verrucous growths or vegetations that thicken the valve cusps and gradually encroach on the outlet and interfere with blood flow from auricle to ventricle.

to reduce pulmonary hypertension by increasing diastolic filling time.

The pathologic findings and the technic of commissurotomy are described by Dr. Effler.

DR. EFFLER: After the patient has been selected and his preoperative preparation completed, the surgeon is assigned the job of correcting a badly diseased mitral valve if it is possible to do so. The evaluation of the mitral valve can be predetermined by the cardiologist to a somewhat accurate degree, but the true extent of damage can be established only by actual examination at the time of surgery by what we call "digital visualization."

as an emergency procedure. Every effort should be made to control all complicating factors prior to operation. The usual measures for control of congestive failure are applicable. Digitalis is not used preoperatively except for the control of ventricular rate in the presence of auricular fibrillation and in the treatment of heart failure. We have used PRONESTYL® for two to three days preoperatively and believe that this in combination with intravenous procaine during operation has been responsible for the prevention of serious arrhythmias during or after surgery. PROSTIGMIN METHYSULFATE® is used routinely to slow the heart rate during operation, and

The normal mitral valve is visualized as a long linear slit not unlike the normal human mouth, with an upper and a lower lip (Figure 1). In the presence of active rheumatic heart disease the valve is burdened by large verrucous growths or vegetations that thicken the valve cusps and gradually encroach on the outlet and interfere with blood flow from

auricle to ventricle (Figure 2). As the disease progresses to arrest and healing, typical full-blown mitral stenosis develops (Figure 3). The lumen is greatly reduced in size, and the commissures are replaced with fibrous tissue. It is quite obvious that this condition will result in tremendous impairment of blood flow from auricle to ventricle, and that there will be a piling up of pressure within the auricle that later will be transmitted into the pulmonary bed.

Technic of Commissurotomy

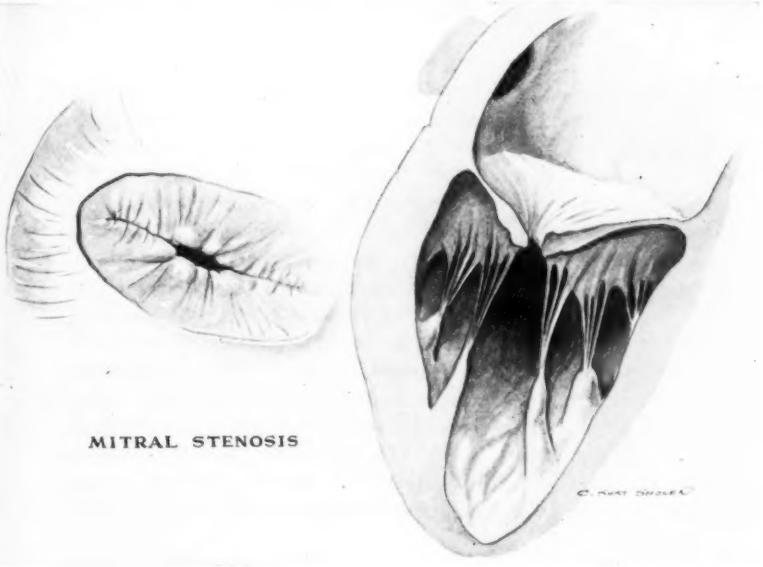
The ideal commissurotomy is any operative procedure that safely can produce the result shown in Figure 4. On the left is what we consider the perfect commissurotomy. The linear slit follows the pathway of or is parallel to the old commissure both to the right and to the left of the buttonhole stenosis. If this is accomplished, the valve will be competent, the stenosis will be relieved, and there should not be burdensome regurgitation.

Occasionally, however, there are calcareous deposits on part of the valve, and an attempt to cut directly through these deposits will frequently result in unfortunate embolization. Thus, when such a valve is encountered we have to be satisfied with a unilateral commissurotomy (to the right in Figure 4). Strangely enough, it does not necessarily influence the prognosis whether a unilateral or a bilateral commissurotomy is done.

A brief pictorial description of the operative procedure as we employ it is given in

POST - OPERATIVE
(top views)

FIGURE 3 *(below)*. Full-blown mitral stenosis. *Left*, the mitral valve as it is approached in digital examination. The lumen is tremendously reduced in size, perhaps one-fifth its normal caliber. The commissures are replaced with fibrous tissue that has approximated the edges of the lip both to the right and to the left. *Right*, a cross section illustrating the thickening of the valve. This thickening is noticeable particularly around the orifice of the valve and less so around the valve leaflet where it is joined to the atrioventricular wall.



MITRAL STENOSIS

FIGURE 4 *(above)*. Ideal result produced by commissurotomy. *Left*, bilateral commissurotomy; the linear slit follows the pathway or is paralleling the old commissure both to the right and to the left of the buttonhole stenosis. *Right*, unilateral commissurotomy; calcareous deposits preclude the performance of bilateral operation.

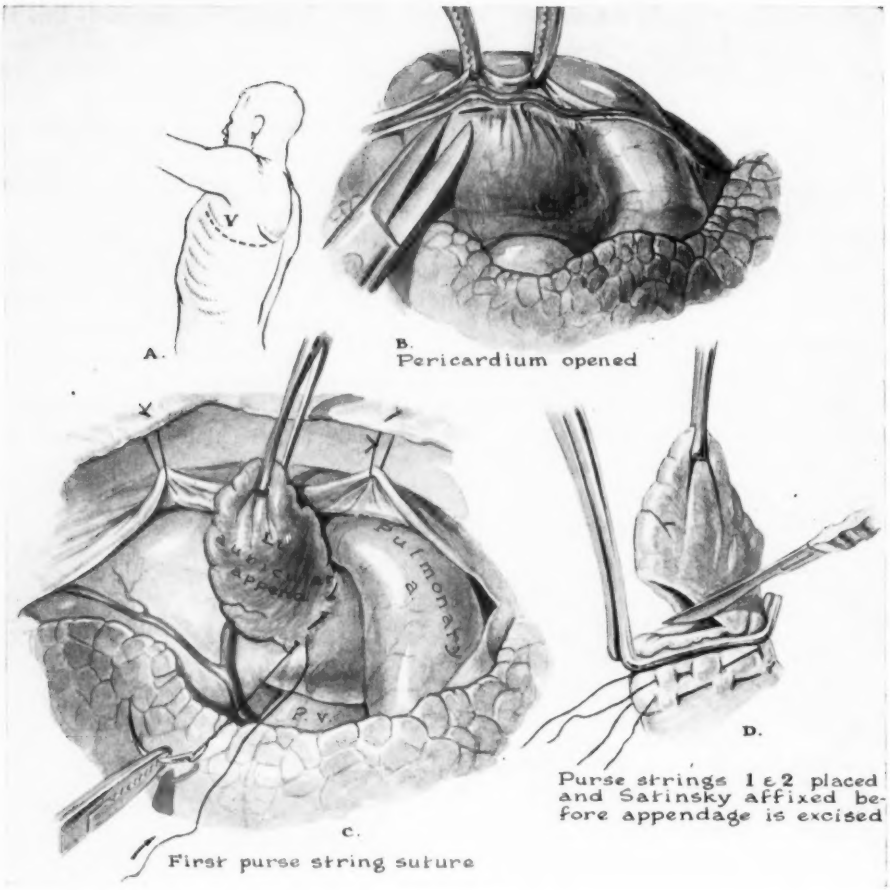


Figure 5. At the upper left hand corner is shown the incision line (dotted line), through the fifth rib or through the fifth interspace. The lung is retracted posteriorly by the assistant, and a long linear incision is made in the pericardial sac, either anteriorly or posteriorly to the phrenic bundle. The pericardium is then pulled away by retracting sutures and the large auricular appendage is mobilized and brought into view. Pursestring sutures are placed around the base, a noncrushing clamp is used to occlude the appendage, and the tip or large portion of it is removed. We believe this will reduce the possibility of an embolus being formed in the atrial appendage later.

Figure 5E illustrates the actual technic of the operative procedure as well as it can be drawn. The surgeon's finger is being introduced into the auricular appendage. If you have a cooperative team that knows its job, the clamps can be removed and the finger introduced into the auricular chamber with the loss of only a few centimeters of blood. The finger then can be used to examine the intra-atrial chamber completely; the presence or absence of mural thrombi, ball valve thrombi, etc., can be detected, and then the valve itself palpated. If there is regurgitation the stream can be felt. The degree of stenosis can be accurately determined with the tip of the finger. Any eccentricity in the valve can be deter-

FIGURE 5 *(left and right)*. Technic of commissurotomy.

mined, and its mobility measured. This is what we call "digital visualization," and it is entirely up to the surgeon's index finger to document the disease accurately as it exists.

Figure 5F is a cross section showing how the finger actually makes contact with the mitral stenosis. Whether you use finger fracture or a knife again depends on the surgeon's choice, but the lines of commissurotomy are demonstrated by the arrow showing the directions of force that are applied to effect the cut or fracture.

When the commissurotomy has been performed, the finger is removed and the auricular appendage is secured at the lower portion of the wound. The entire operative procedure should be accomplished within a reasonable length of time. We usually allow approximately one and one-half hours for the complete operation from opening to closure.

Postoperative Care

DR. SONES: The postoperative period of hospitalization varies between 10 and 18 days, and averages two weeks. After discharge the patients follow a bed and chair regimen for two more weeks and then gradually increase their activity, being careful to stay within the limits imposed by their own fatigue and shortness of breath. Usually three months pass before they reach maximal activity tolerance; in some cases this period is longer. During

FIGURE 6 *(left)*. Roentgenogram taken on the day before commissurotomy was performed (Case 4). The heart is enlarged approximately 10 per cent, and there is evidence of left auricular and right ventricular enlargement, characteristic of pulmonary hypertension.

FIGURE 7 *(right)*. Same case as Figure 6. Roentgenogram made three months after operation. The heart size and configuration are within normal limits.

this time recurrent episodes of pleural and neuromuscular chest pain are not uncommon. These usually are self-limited occurrences and are not dangerous, but they may be distressing to the patient.

All patients are kept on a low salt diet during the first three months after operation. This is then discontinued if congestive failure was not present prior to commissurotomy. Salt restriction may be continued indefinitely in group 3 patients.

Heart size may be essentially unchanged after operation, but in most patients who undergo commissurotomy before the onset of congestive failure, it is significantly reduced.

Over 90 per cent of the entire group of patients who have been observed for periods longer than six months since operation continue to show remarkable functional improvement. These subjective gains have been substantiated by objective studies which have included cardiac catheterization in many instances. On this basis it now seems reasonable to anticipate long-term reduction of morbidity and improved life expectancy by the effective use of a combination of medical and surgical management of patients with mitral stenosis.

Case Reports

Case 1—A 42 year old woman had had dyspnea since the age of 17 years. Intermittent orthopnea had been present for 20 years prior to operation. Commissurotomy was performed in June 1951. Immediately after the operation, the patient stated she could breathe a lot better. She had been bedridden for nine months prior to operation. For five or six years she had slept on more than two pillows in order to breathe. About six months were required after surgery before she felt completely well—before she could spend a full day downtown shopping.

Case 2—A 46 year old woman had been unable to work for a year prior to operation; at present she is employed as a saleslady in a department store. She stands all day, and makes frequent business trips.

Case 3—A 40 year old woman had a history of exertional dyspnea for about 15 years prior to operation. Commissurotomy was done in May 1951. Prior to surgery she had been unable to do housework or shopping. She is a baseball fan, and stated that two and one-half months after operation she attended a game with her husband, and had no difficulty in walking up to their seats.

Case 4—This patient, a 37 year old woman, was what we call the ideal candidate for commissurotomy. She had been unable to lie down for two years and had been ill for a much longer time. A roentgenogram taken the day before operation showed about 10 per cent cardiac enlargement and clearcut evidence of left auricular and right ventricular enlargement, which is so characteristic of pulmonary hypertension (Figure 6). Figure 7 was made three months after operation. The heart size and configuration are within normal limits. Three days after the operation the patient was able to lie down. She is now able to do all her own housework.

Case 5—A 50 year old man had not been able to keep a steady job for 15 years, and had managed economically only by doing odd jobs for short periods of time. During one five month period he was hospitalized seven times. About a year ago commissurotomy was done. In the past six months he has not lost a day of work. He still takes digitalis once a day, but has had a fine result from operation.

Differentiation of Precordial Pain

GEORGE SAMUEL BOND*

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The differential diagnosis and evaluation of precordial pain at times are very difficult. One reason for this is the fact that there are no objective signs to help in making the diagnosis, and one has to depend entirely on the pain itself. Consequently one must be sure that he gets a careful statement regarding all the factors related to the pain. Also, all pains in the precordial region have the same mechanism; consequently, regardless of cause, the pain itself is exactly the same and may have the same distribution and character. Many things cause pain in this region if it affects this same reflex arc, and one must determine the background cause.

GEORGE SAMUEL BOND

PRECORDIAL pain represents in many instances an extremely serious condition, and it is therefore necessary that a very careful analysis be made in every case to determine the cause. I will not attempt to discuss all the possible causes or the various types, but I will mention some which are the most important and the most difficult to differentiate.

The problem of diagnosis in precordial pain is mainly that there is nothing to back up the diagnosis except the pain itself. A patient with appendicitis has pain, but he also has rigidity, fever and other symptoms which tend to give a background that differentiates the pain from other types that might occur in similar places. In contrast, many patients with serious coronary disease may present no findings whatsoever except for the pain. Blood pressure, pulse, heart size, heart rate, electrocardiographic findings both before and after exercise, and results of functional tests of various sorts may be normal, and yet the patient may die within a week or two, still with no symptoms other than precordial pain. Consequently one has to depend on the patient's statement concerning the pain, and this requires that every minute factor relative to that pain be evaluated—the time it is brought on, the way it is brought on, the degree of pain, what makes it quiet down and where it radiates.

I would like to emphasize a couple of points with regard to the complete history which must be taken. First, be sure you know what the patient means. Often, symptoms do not correspond in the patient's mind with what the doctor thinks the terms imply. For instance, take the word "headache." If you were to ask several persons to define a "headache," you would probably get as many different answers as there were persons answering the question. Therefore you not only have to take the patient's statement of the symp-

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

tom but also must inquire specifically as to just what he means by that symptom.

Some years ago a patient was admitted to the hospital with a diagnosis of angina. The resident went in to see him and came to me saying, "I can't find that this man has any symptoms suggesting angina. He doesn't even complain of any pain." I questioned the patient and found that he had gone to the doctor's office complaining of misery in his chest. The doctor immediately assumed that "misery" meant pain. As it turned out, the patient simply had a feeling as if everything dropped out in his chest every once in a while, and it was found that he had an innocuous extrasystole. You have to be certain that you know exactly what the patient means when he tells you he has pain.

Secondly, you have to size up the patient, and I think this is very important with the anginal group. So much of your interpretation of the pain as a symptom depends on the type of patient you are dealing with. If a stoic individual, a man about 65 years of age, comes in and says, "Doc, I have a little soreness that comes up once in a while in my chest," you had better be careful. On the other hand, if a neurotic person complains bitterly of pain, then you can discount to some extent its significance. Sizing up the patient and making your interpretation fit the type of person with which you are dealing are important in making the diagnosis.

Precordial pains are all referred pains. The arc is similar in all cases. Certain sensations pass up through the sympathetic ganglions in the chest to the cord and are then referred out to the integument of that same segment of the skin as a pain sensation. I want to emphasize the importance of this. Whether the heart is producing the pain or whether it is the result of other causes, the same reflex arc is brought into play and the pain is the same. Consequently you cannot expect differences in distribution; this may be the same. Pain due to various causes may occur in the same or in several different locations. You cannot expect differences in the pain itself which will tell you that one is due to one cause and the other to another. It is true that in some instances there are predominant factors emphasizing the pain in one location or of a certain character, but unfortunately there are just enough exceptions to the rule to make diagnosis difficult.

Certain factors in the production of the pain might change its character because of the different sensory phenomena that are sent up. These changes in character may be used to determine causes, but the pain itself cannot be differentiated because all types of precordial pain utilize the same reflex arc.

We will consider first the paroxysmal pains in the precordium. Before going into the organic types I want to say just a word about pain that has no organic basis, one of the most troublesome to differentiate. These are purely psychogenic pains in psychoneurotic individuals, and they have no organic basis whatever. An example was a man I saw many years ago who had attacks of severe pain across the sternum and down the arms, lasting 3 to 6 hours every day. When I first saw him, he had had these attacks for 2 or 3 years, and I observed him for a similar period of time. The pains were terrific, and it was obvious that if he had had that much pain due to anything organic as far as his heart was concerned, he would not have been alive. The clues to the situation evolved from the facts that he was a neurotic individual and that his attacks had begun just after he saw his father die of a true coronary thrombosis. After that incident, he had had daily pains which nothing would relieve.

The patient we have here today is a 56 year old man who had been perfectly well all his life until a year and a half ago when he noticed slight pains across the upper half of his chest, together with a sense of tightness. The pain was associated with exertion and was relieved by rest. The attacks lasted 2 or 3 minutes and occurred about once a day. Then the patient noted that excitement as well as physical exertion would bring on an attack. The attacks became progressively more severe and frequent, and about 2 months ago, following an acute upper respiratory infection with the development of fibrillation in his heart, they began to last 15 or 20 minutes

and to occur several times a day. Still, however, they followed the pattern of exertion.

He then noticed that eating played an important part in production of pain. About 2 months ago this became so pronounced that he could not do anything for about 2 hours after a meal. During the past few weeks the pains have occurred at night, with no relation to exertion, and just before he was admitted to the hospital there were times when he sat up all night because of the pain.

The pains were felt in the upper half of the chest, equally on both sides, and extended across from shoulder to shoulder and up into his neck and jaws. There was no sensation of pain in his arms, although he complained of a feeling of heaviness and numbness, with tingling. He described the chest pain as a heavy ache, not a sharp pain at all, but a very serious one.

This man had no symptoms other than the pain. He has been somewhat short of breath during the attacks since fibrillation developed, but this finding is present also between attacks. There is some sweating with the pain, but no signs of collapse. There is no nausea. During the last month or so he has noticed that breathing aggravates the pain. Some of the shortness of breath probably is due to the fact that it hurts to breathe, rather than to true dyspnea.

The physical examination is essentially negative. His blood pressure is 190/120. The heart is somewhat enlarged. There is a loud systolic blow at the apex. Auricular fibrillation is noted both on physical examination and on electrocardiographic study. With the possible exception of the shortness of breath, there are no signs that indicate decompensation. Aside from the fibrillation, the electrocardiogram is essentially normal.

This man represents the true, simple picture of a coronary angina. His pain, as in most of these instances, is substernal, radiating to the two sides and into the arms in the form of pain or the subjective sensations described. This patient has pain in both arms, but in most cases the left arm only is affected. In about one-fourth of the patients it is present in both arms, and in about 1 out of 25 the pain is referred to the right arm only.

The pain is a rather dull, heavy ache, often a sense of pressure more than an actual sensation of pain; it may, however, be excruciating. A few patients describe it as burning in character.

In the majority of cases the pain is due fundamentally to something that increases the workload of the heart. It is an exertional pain. In that respect let me stress one or two points. When you are determining how much exertion causes pain, consider the factors that modify the amount of exertion. Seasonal factors are very important. In winter much more clothing is worn; walking conditions are much more difficult, with heavy, cold winds and peripheral constriction. In summer, things are much easier, and a person may have pain in winter and not in summer. That is not a bizarre finding; it is simply that physical exertion is greater in winter. Also, exertion may vary under different conditions; e.g., pleasurable activity is often done with greater ease than work. One man, for instance, who had a great deal of pain one morning when he was painting a fence found he could paddle a canoe all afternoon with no pain at all.

Excitement also often changes the pain reflex; an individual may have no pain when he does a thing under excitement and yet will have pain with the same amount of exertion when he quiets down. Anything that requires lifting the weight of the body in addition to the job being done increases the pain; examples are walking uphill and climbing stairs. The type of work a person is accustomed to doing may determine whether or not he has pain. Some men can swing a sledge hammer without having pain, whereas others will have pain associated with much less strenuous activity, and yet the two would be comparable as far as the amount of exertion is concerned. Eating makes a difference; after meals it is much harder to do the same amount of work.

Early morning seems to be a particular time when pain is produced by lesser amounts of activity. I do not know why, but often for an hour or so after a person gets up he is unable to do anything without producing pain, and yet during the rest of the day he can do

about as he chooses. Some people have pain on the first exertion of a kind; e.g., they can play the first hole of golf and have pain, and then play the rest of the game without any more pain. Others tend to have pain with comparable exertion no matter how many times they have done it before.

Lastly, emotional factors play an important part both in producing the pain itself and in helping to exaggerate it. Consequently, an individual who exerts himself may have pain if he is under stress and yet if he is quiet and calm he will have no pain during the same amount of exertion.

The effect of work on the heart produces pain as a result of lessening the circulation, with muscle ischemia in proportion to the amount of work done. Normal hearts can exhibit angina if the work is sufficient. Every person probably has had angina some time in his life. If the work is excessive, such as in athletes, the normal blood supply to the heart is not sufficient to take care of the added strain. Such a person has exactly the same relative conditions that are produced in a person with true angina. On the other hand, patients can have pain from heart effort without physical effort. This is seen, for instance, in the precordial pains that occur in anemia; it is seen in the tachycardias; it is seen in hyperthyroidism. All these conditions, which result in more heart effort for a given amount of physical activity, will produce pain just as if the work had been excessive.

The most important cause of pain, however, is diminution of the coronary blood supply due to coronary narrowing, as a result of which pain is produced by small amounts of physical exertion. The other causes mentioned are not primary cardiac pathology, so if pain is produced by an insufficient amount of heavy work you can be sure that the blood supply is reduced and the condition is coronary in origin.

Several types of pain simulate coronary pain. In the gastrointestinal tract, many conditions produce pain which may simulate that of coronary disease. Ulcer usually is not too difficult to diagnose; the location of the pain, the conditions that produce it, its relation to eating, the type of pain and the relief obtained probably will make the differentiation clear. In gallbladder attacks it is harder to differentiate because the pain distribution may be the same as in coronary disease. There may be evidence of gallstones, but these do not always produce pain. However, gallbladder disease is usually associated with other gastrointestinal symptoms, and abdominal findings tend to show that the pain is originating below the diaphragm rather than above it. Indigestion and gas are common causes of pain in the precordial region, and unfortunately these conditions themselves may precipitate the pain in true coronary disease. Consequently one has to determine in each instance whether the condition primarily involves the stomach or the heart. Often that cannot be done on the spur of the moment, but after a few weeks of study, analysis of the pain and of conditions under which that pain is produced will point either to the heart or to the stomach as the probable cause. In abdominal disease the attack lasts longer, there is evidence of gastric gas, and gastric distress and abdominal distention help make the diagnosis.

One of the most difficult differentiations is that of the spastic states in the gastrointestinal tract. These conditions may be in the esophagus, cardia, pylorus or even the transverse colon. The pain occurs at any time and as a rule is not related to exertion. Attacks often occur at night. The pain, which may be severe, is rather diffuse in the chest, and lasts a great deal longer. It is not relieved by rest, but often the patient is more comfortable if he gets up and walks around. These spastic states can sometimes be shown roentgenographically, but unfortunately the spasm may not be present just at the time the x-ray is taken and in consequence it may be missed. If the spasm is noted on the x-ray, of course, it helps the diagnosis substantially.

Hiatus hernia may produce a picture very similar to angina, but we will not have time to take that up in detail. The fact that it may be more prominent when the patient is lying down and that it tends to subside when he gets up, which is just the opposite of angina,

often helps to diagnose the condition.

Another group who present difficulties in diagnosis are those with nerve root pains. If these pains occur in segments of the cord which involve the precordium, they may simulate very closely those due to coronary disease. One difference is that these pains are usually quite sharp and stabbing in character, rather than the dull, heavy ache of true angina. Also, these patients tend to have soreness or tenderness in the intervals between attacks of pain, which is not at all characteristic of angina. Exertion as a rule does not cause the pain, but one may be fooled, because if a man has a disk or some compression in the vertebrae, when he walks he will tend to have pain from that condition. This is apt to be mistaken for an effort type of heart pain. However, one can distinguish this because the pain is primarily due to jarring; in spinal conditions the patient will have the same pain if he sits in an automobile and rides over a rough street or if he does anything in the way of movement of the spine. Even in bed the pain will come on if he changes his position. It may come on while he is walking.

A point of importance is that nerve root pains are very definitely segmental. In a patient who has cardiac angina, the pain radiates in different directions and does not follow any segmental distribution. The pains in all nerve root conditions tend to follow certain nerve segments and will be confined definitely to those segments. Also, in nerve root pains there is a tendency for sensory disturbances to continue between attacks of pain.

These nerve pains may be any one of 3 types: (1) True nerve pains, intercostal neuralgias or neuritis, or any condition which may involve the nerve itself is very apt to occur in women, especially young women, and to simulate the true anginal picture. However, if one presses on the nerves in that region between the paroxysms of pain there is nearly always a residual nerve tenderness which will differentiate the pain from true angina, in which there is no such tenderness between attacks. (2) Radiculitis may have to be differentiated, and it can, as a rule, by the tender points of emergence of the nerves at the spine and hypersensitiveness in those particular areas of the skin. (3) Disks, vertebral degeneration, compression fractures, etc., may give the same picture, but here there is definite evidence of segmental distribution of the pain with paresthesias and disturbed sensations in the area as well. X-ray of the spine usually brings out the possibility of a nerve condition rather than a true cardiac condition.

Pain of the paroxysmal type is very difficult to diagnose, and the closer you analyze to determine whether the patient is suffering from a serious anginal condition or from another less serious one, more amenable to treatment, the more good you do for that patient.

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GENERAL PRACTICE *Review*

Psychotherapy in General Practice

EDWARD WEISS*

Temple University Medical School, Philadelphia

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

EDWARD WEISS

WHEN a patient comes to a psychiatrist he comes prepared to discuss his emotional problems, but when he consults a general physician he is almost always looking for a physical cause for his trouble. But in at least one-third of all patients with chronic illness who consult a physician no definite bodily disease can be found to account for the illness, and in another one-third of such patients the symptoms are not explained by, or are out of proportion to, any organic disease that can be discovered. Therefore in a very large group of patients that every physician sees there is a factor other than physical disease that is making them sick and this factor is usually emotional. How to deal with this from the standpoint of diagnosis and treatment is the special point of this paper.

Psychosomatic Diagnosis

When a person gets sick he is sick all over; that is, the body and mind are one, and he gets sick for a variety of reasons, physical and psychologic. In other words, it is usually not one thing that determines illness; there are multiple factors acting together. Therefore, in our approach to illness, as Halliday[1] states, we must consider: 1. What *kind* of a person are we dealing with (inherited and acquired characteristics, physical and psychologic)? 2. What has he *met* (germs, allergens or emotionally disturbing events)? 3. What has *happened* (the physiologic mechanism or pathogenesis of the disorder)? For example, allergic responses occur when a prepared organism, possessing certain physical and psychologic characteristics, meets certain elements, physiologic and psychologic. In some allergic disorders a single preponderant factor may be largely responsible, as for example in pollen hay fever. In others, such as asthma, there are frequently multiple interrelated factors, allergens and emotional disturbances, which act in a complementary fashion to produce the disorder.

Therefore, in the study of the sick person we must pursue our usual physical and laboratory investigations, but in addition we must get to know the person in the patient—in other words, understand him as a human

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being rather than just as a medical case.

Just as I insist on this unity regarding the nature of illness—the body and mind are one—so do I urge that the means of investigation are two: physical and psychologic, and their simultaneous application represents psychosomatic diagnosis. Moreover, they are applied simultaneously, although their application is often unconscious and unscientific. In our usual approach to the patient, using orthodox methods of medical history, physical examination and laboratory studies, we at the same time make many intuitive observations about the unconscious mental processes of the patient as exhibited in his language and behavior. What I am suggesting is that order be brought into this intuitive process. Rather than be satisfied with loose terminology—neurogenic factors, emotional upsets, physical and mental fatigue, emotional stress and strain—we must make an effort to define the specific emotional problem and relate it to the total personality makeup of the patient.

How do we do this?

1. First of all *the nature of the symptoms* themselves often suggests an emotional background for the illness. The patient who says, "I hardly know where to begin," when asked about his trouble and then goes on to talk about fatigue, vague aches and pains, restlessness, irritability, sleeplessness, and a host of other symptoms that we recognize to be commonly of neurotic origin makes us suspicious that we are dealing with illness of the same origin. However, we must never forget that the neurotic patient can have a disease so that we must have one foot planted as firmly in tissue pathology as the other is in psychopathology in order to stand on safe ground in diagnosis.

2. *A family history of psychopathology*—Neurotic difficulties arise in the family group, and therefore in taking a history we must try to determine whether there is emotional instability or maladjustment among members of the family from which the patient came. Broken homes, divorce and separation, alcoholism, as well as a history of "nervous breakdown" among blood relatives, suggest the kind of background that produces neurotic difficulties.

3. *Evidences for a childhood neurosis*—Neurotic and psychosomatic difficulties do not usually arise in adult life without some indication of emotional troubles earlier in life, so that when behavior disorders such as bedwetting, nail biting, nightmares, etc., persist or are very pronounced they suggest that we are dealing with an individual who carries a heavy burden of anxiety in his makeup.

4. *Neurotic character structure*—As we study the longitudinal life history of the individual we get further evidence of his emotional maladjustment, often in relation to work, social life, and love affairs. Almost never does a symptom of emotional origin exist alone. There are usually other evidences of personality difficulties.

5. *Specificity of emotional factors*—When we cross-section the life history at the time that the symptoms began we will frequently find an emotionally disturbing event that is specific for the particular personality. If the person is heavily predisposed because of a large burden of anxiety the emotional factors that precipitate illness may be trivial; if better adjusted, a major catastrophe may be necessary to precipitate neurotic or psychosomatic disturbance. In either event the incident is specifically related to the particular personality.

6. *Demonstration of significant behavior*—When meaningful material is touched on in taking the medical history the evidence in the patient's behavior is unmistakable. We must, of course, allow for the stress incident to the first contact between patient and physician, but usually there is no difficulty in determining from the patient's behavior that what we are discussing has a special meaning for him.

7. *Hyposensitization by psychotherapy or by the avoidance of provocative situations*—As the patient talks about the problem that is disturbing him he often improves, and this is further confirmation that the diagnosis of neurosis or "functional illness" is correct. We must remember that improvement may be more obvious to the physician and to the family than to the patient. A patient often

denies that he is better while members of his family attest to his improvement. It is better to ask such patients, "What have you done?" rather than "How do you feel?"

Physicians often ask, "What can you do about the patient who refuses to talk or states that he has no emotional problems?" I often encourage patients to talk about their problems by homely analogies. I say to them that they are like a teakettle on the stove. If the steam comes up and can't get out the spout it tries to blow the lid off. This suggests that tension of emotional origin is like steam under pressure; it must get out somehow, and if it doesn't get out by word or deed it backfires or short-circuits and disturbs the working of the body. Thus patients begin to realize that the best way to deal with tension is by action; the next best way is by speech, and the least satisfactory is by thought. So that we can say to them that if they cannot express their tension by word or action, if they cannot say with their mouths what is disturbing them, then one of their organs will try to say it for them with a kind of "organ language." Thus, the patient with nausea, who has no evidence of organic disease, may be indicating that he cannot "stomach" certain situations; the patient with an itch often "lets things get under his skin." Many additional examples could be given[2] to show that the patient often expresses his body language in symbolic formulas if we would only listen to him.

Another satisfactory way to get patients to discuss themselves in relation to their illness is to use a case illustration. Repeatedly this is effective when other methods of trying to make patients see the relationship between emotions and illness fail. If the physician can think of an apt case illustration the patient can readily identify himself, and even if there are pronounced divergences the patient will often see a partial application which will encourage him to talk about his personal life. Sometimes he will deny the application only to go on from that point to discuss emotional factors of importance which previously he was unable to think of.

History taking—An important element of the doctor-patient relationship enters into the taking of the history. I cannot discuss all the qualifications of the physician who should interest himself in psychosomatic problems. Here it is only necessary to say he must be so constituted that he can listen to the patient uncritically. Sympathy for patients suffering from illness of emotional origin is an essential part of the equipment of the physician who would interest himself in psychosomatic problems. If he is unsympathetic it will show in his manner and will discourage the patient from revealing feelings that are essential to an understanding of the problem.

The introduction of the psychosomatic point of view does not require a different form of history taking; it only requires an awareness of the role that the emotions play in illness and hence more emphasis on certain aspects of history taking. *Thus the history need not differ in form but it must differ in substance.* In accordance with what has been said, more attention will be paid to the behavior of the patient and to the actual words that he uses in describing his complaints as well as to the asides and apparent irrelevancies that so often give important clues to the emotional factor. Another fundamental consideration is to give the patient time, allowing him to talk with as few interruptions as possible. This, of course, is one of the great problems, the matter of time. Certainly the average physician cannot be expected to take an hour of his time during a busy office hour to study the life history of a neurotic patient or one whom he suspects is neurotic but time is the essence of the problem. There are no shortcuts in history taking; while the experienced physician may quickly grasp the situation, time must be taken because the patient cannot be hurried. Therefore, with the occasional patient in whom this approach is essential a special appointment can be made so that time can be taken to listen to the patient's story. In the end, it will prove economical both in the saving of dollars and in human suffering. Many patients with "thick charts" have spent a fortune accumulating a sheaf of documents, but with an end result hurtful rather than helpful because the diagnosis was

obscured by concentration on parts rather than on the whole.

Psychotherapy

Patients do not have to be told, "You are now undergoing psychotherapy." What we must do can be done in the usual relationship between physician and patient: (1) After a medical history, which takes account of personal factors as well as "medical facts," we should make a complete physical examination and such laboratory tests as are necessary to exclude physical disease or to establish the precise nature of the organic problem and the amount of disability which it in itself is capable of causing. (2) When the patient has been assured that there is no physical disease or that disability is out of proportion to the disease, it is usually easy by examples of psychic causes for such physiologic disturbances as blushing, gooseflesh, palpitation and diarrhea to make the patient understand that a disturbance in his emotional life may be responsible for the symptoms. (3) Continue to look for the person in the patient. The more one can persuade such a patient to talk about "his other troubles" the sooner does one come to an understanding of the "present troubles." The greater the success in switching the conversation from symptoms to personal affairs, the sooner does one come into possession of the real problem disturbing the patient. Encourage him to talk about himself as a person rather than as a medical case.

Usually one or more of three special fears are uppermost in the minds of such patients. One of the most common is fear of *cancer:* cancerphobia. A great many patients think they have cancer, and indeed most women who consult physicians will have the idea at some time. They do not always express it; in fact, they rarely directly express their fear of cancer. They often disguise it by a complaint about a lump, a swelling or a curious sensation in the abdomen or breast, and when they are assured at the end of a complete physical examination that they are free from organic disease, they heave a sigh of relief and say, "Oh, I am so glad because I thought I might have a cancer." With all of the propaganda for the early detection of cancer these fears are exaggerated, and I presume it is the price that we must pay for instructing people about cancer. I am not, of course, advising against such instruction; it is only that we must realize that we add to the apprehension of many patients by our emphasis on the early detection of cancer.

Another common fear is of *heart disease.* When pain in the precordial region as well as rapid beating of the heart, breathlessness and fatigue occur, suspicion of heart disease often arises. If it is remembered that the pain of cardiac neurosis bears no definite relationship to effort, is frequently described as sticking, needle-like, or soreness, that often it is associated with inframammary tenderness and hyperalgesia, so that the pressure of the stethoscope sometimes elicits it, and that it may be accompanied by a sense of choking as well as sighing respirations, there will be no difficulty in the differential diagnosis, particularly when these symptoms are associated with the whole picture and life situation of the person with cardiac neurosis.[2]

The problem is not an easy one because the patient is apt to insist, "But there must be something the matter." He cannot understand that so much distress can occur unless some vital organ is seriously affected. Moreover, if one does succeed in reassuring him for the time being, he may continue to hold the reservation, "But if this sort of thing continues surely something will happen"; in other words, "How long can my heart stand this?" Telling the patient to control himself is like trying to hold back steam under pressure—if it does not come out the spout it tries to blow the lid off the teakettle. Really a person is quite as incapable of controlling his anxiety as he would be incapable of controlling his own acutely inflamed appendix. As long as the discussion is kept on the level of trying to persuade him that he does not have physical disease or of giving another prescription for phenobarbital, one gets no place because one cannot argue with an obsession nor eradicate it with a drug. One must get at the mixed feelings, the conflict, that underlies the anxiety, and this can only be done by encour-

aging the patient to talk about his personal problems.

The inability to concentrate often gives rise to the fear of "losing the mind." Along with this fear frequently there are ideas of suicide. Both are distressing to the patient and usually are not volunteered. When the patient is assured that it is his feelings which are involved and not his "mind" and that the reason his "memory fails him" is because he is so preoccupied with concern over his problems, then he may confess his fear that he was "losing his mind" or his ideas of doing away with himself.

Once these ideas are brought to the surface and ventilated, and the patient receives sufficient reassurance, then often much improvement occurs. Indeed the intensity of the fear and the amount of reassurance necessary to abolish it serve as a crude index to the depth of the neurosis.

It is a good rule to listen rather than to talk. Giving advice on highly charged emotional matters is dangerous. To paraphrase Lindemann,[3] "Clumsy psychotherapy is as dangerous to the social life as clumsy surgery is to the physical life."

People frequently try to blame their illnesses on "something they et." I say, "No, it's probably something you met." And so often it is true that the life situation has precipitated the trouble but instinctive tendencies place the blame on something swallowed; i.e., the food eaten at the time. In the same connection, people are gullible about wanting a cure by "swallowing" some magical medicine—vitamins, for example. I say to them, "The cure is not in swallowing; it's in spitting out"; in other words, talking about some of the things causing the trouble.

Pregnancy and parenthood—It is not unusual for physicians to recommend pregnancy and parenthood as a cure for neurotic and psychosomatic illness. This prescription is rarely, if ever, of value. It is a rather safe rule that the unstable person will not be helped by becoming a parent, but will usually be made worse as a result of the added responsibility. How often on taking the history of a neurotic woman does one hear, "I was perfectly well until my first child was born, but I haven't had a well day since." It is true that some neurotic women will feel better during pregnancy, but they pay dearly for their short period of improvement. Nor should the cost to the child be forgotten. Not only does parenthood not cure neurosis but it prepares the way for another spoiled life, because this is surely one of the ways in which neurosis is perpetuated. The atmosphere of the home in which there is serious emotional maladjustment is the culture medium for the development of further emotional problems. This is the real "social disease." Psychologic contagion is as important as germs in causing illness. The advice to an incompatible couple—"What you need is a child; then you will have a common interest"—is as unenlightened as it is dangerous. While it may succeed in holding the marriage together, who can say how many children are thus sacrificed on the altar of incompatibility?

The anxiety attack—Rather frequently the first pronounced evidence of neurosis may be an attack of anxiety, and again and again in studying the histories of patients with chronic invalidism of emotional origin one finds that the first outspoken manifestation of illness was the sudden onset of anxiety with apprehension and dread. There are a feeling of weakness, sweating and a sensation that something terrible is about to happen. There are dyspnea, palpitation and, sometimes, nausea. The attacks usually last only a few minutes and subside rather quickly but may last for an hour or more. Weakness and fatigue follow. The emotional as well as the physical distress is so pronounced as to cause the patient to conclude that some serious physical disability is present. Almost never does he conclude that his difficulty is emotional. Most people prefer to think that physical distress means physical disease, and unfortunately physicians too frequently have assisted them in this belief.

When a patient with an acute attack of anxiety is first examined, the physician notes the rapid pulse and listens to the pounding heart and all too often permits the patient to believe the heart is diseased, or that hyper-

thyroidism is present, or covers his unwillingness to make a diagnosis of a psychologic disorder by using some such term as neurocirculatory asthenia or autonomic imbalance. To give drugs and do nothing about fear is to mislead the patient into feeling that his distress is due to a physical disease rather than to an emotional disorder.[4]

What is psychotherapy?—What, indeed, is psychotherapy? Too often it is assumed to be "the application of the art of medicine." This defies analysis but seems to represent something called "common sense" and the generous use of sedatives, placebos and reassurance. The psychologic approach in medicine, essential for psychotherapy, consists of something more. It is an effort to understand the personality structure of patients, the mental mechanisms which are at work and the specific relationships of psychologic situations in the precipitation of the illness.

Reassurance, in the majority of instances, unless combined with an analysis of the illness from the standpoint of the behavior, gives only temporary help and, depending on the degree of anxiety, has to be repeated constantly, like a dose of digitalis in a failing heart. Closely allied to reassurance is another superficial treatment that rarely results in more than temporary help; i.e., environmental manipulation, without any attempt to give the patient insight into his conflicts.

Real psychotherapy, which is directly the opposite of simple reassurance, tries to make the patient understand the meaning of his symptoms and the nature of his conflicts. It is a process of re-education and, when properly done, leads to sufficient emotional development so that the necessity for symptom formation is abolished.

Major and minor psychotherapy—A considerable number of these patients cannot be sent to psychiatrists, nor is it necessary. Not that there is anything reprehensible about consulting a psychiatrist—this too is a problem of education—but there are not enough psychiatrists to take care of the thousands of patients, and moreover, as I have tried to show, a great part of this work lies in the field of general medicine. Another way of stating the problem is to say that there are a major and a minor psychotherapy just as there are a major and a minor surgery. The general physician must be able to treat the minor ailments, but he must be able also to recognize when the problem is beyond him, and then refer the patient elsewhere for major psychotherapy.

The more the cause of the illness lies in the environment the more likely that the general physician will be able to handle it, and of course the more the problem lies within the patient and the less disturbance there seems to be in the environment the more the problem belongs to the psychiatrist.

One might summarize minor psychotherapy in these points:

1. Give the patient time to tell his story; listen rather than talk.

2. Get to know the patient as a person rather than just as a medical case; look for the person in the patient.

3. Make the physical examination (including laboratory studies) as complete as necessary; exclude or evaluate physical disease.

4. Reassure him that there is no evidence of cancer, heart disease or mental disease.

5. Explain to the patient that he has a disorder and not a disease (i.e., "irritable colon" not "colitis"); that symptoms are real (not imaginary) and although unpleasant will do no damage to the body.

6. If disease is present, explain that the symptoms are out of proportion to the disease (for example, the headache and fatigue in hypertension).

7. Look for and explain the time relationship between onset of illness and emotionally disturbing events.

8. Encourage discussion of personal problems: family setting, marital situation, work, social life.

9. Ask the patient to give his own explanation of his illness and re-educate him on the mechanism of symptom formation: how tension of emotional origin causes symptoms.

10. Instead of cautioning rest, urge the patient to engage in more work and social endeavor. "Carry on in spite of symptoms." This externalizes psychic energy (libido) and di-

verts attention from body sensation.

11. If drugs are used, explain their action; avoid "mystery."

12. Try to desensitize, by repeated discussion, against noxious environmental influences: unfriendly relatives, critical employers, etc. If desensitization is not successful and modification of environment is impossible, then change of environment is indicated.

Cost of psychotherapy—What about the question of time, effort and expense of psychotherapy? True it is that all of this takes time and effort and must be paid for; yet when one looks into the time, effort and expense that have been expended by many patients or by institutions taking care of these patients in the usual medical approach, one realizes that an hour or two well spent in a discussion of the life situation of such patients would obviate a great deal of this expense. It is amazing what the total expense of a great many of these unnecessary studies amounts to so far as the institution is concerned, and of course the same thing is true in the case of private patients. The day is close at hand when we will regard some of these "thick chart" patients, this polyphysical approach, with the same amusement and disdain with which we now regard the polypharmacy of a bygone age in medicine. Hospitals are beginning to understand that it is not only intelligent but also economical to utilize the service of a psychiatrist in the general medical division, and this same idea can be applied to private patients, with this difference, that the majority of them can be and should be handled by the general practitioner. But he asks, "How can I possibly take the time to do this and, if I do, how can I make a living?" I answer that it is not necessary, of course, to make such a detailed inquiry in every patient that one sees, but, in chronic illness in particular, when one feels the necessity for such a study, time must be taken and in the end will prove economical not only from the human standpoint but also from the standpoint of the cost of medical treatment. It will be worth while as far as the health of the patient is concerned and in satisfaction to the physician.

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Carcinoma of the Cervix

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About 20,000 women in the United States will die of cancer of the uterus this year. The condition is responsible for 17 per cent of all cancer in the female and for 95 per cent of all female genital cancers. About 0.5 per cent of women eventually have cancer of the uterus.

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The foregoing statistics are impressive and present a real challenge to all practitioners as well as to those who are primarily interested in the field.

Early Diagnosis

Since very little is known concerning the etiology of uterine cancer, probably nothing can be done to lower the incidence. However, as we shall attempt to show in this presenta-

tion, a definite and consistent lowering in mortality rate can be expected. Encouragingly good results can be obtained in the earliest stages. Therefore, not only must such cases be found and diagnosed early, but proper treatment has to be instituted immediately.

PAUL N. LARSON

As with breast tumors, much publicity about early detection of uterine cancer is being given. Also, prophylaxis by the physician, through finding early phases of carcinoma of the uterus, is very important.

Pelvic examination—Granted, the physician can do little more than educate women to come for an examination, but how many doctors allow the patient, when she is already in the office, to postpone a pelvic examination because she is bleeding? That is exactly the time and the patient for the investigation. The cheapest insurance a woman of 40 to 50 years of age can have is a pelvic examination every 6 months.

The physician should take time to reconsider the value of a thorough pelvic investigation. For if cancer of the uterus is to be diagnosed early, the lesion must be looked for at every opportunity. An adequate pelvic examination should include:

1. Careful palpation and inspection of external genitals.

2. Speculum examination of vaginal vault, being sure the cervix and mucous membrane are cleansed.

3. Bimanual palpation of cervix, corpus, adnexa and cul-de-sac; also of the rectovaginal tissues. (Empty rectum in questionable cases.)

4. Biopsy of suspicious cervical areas.

If the bleeding is abnormal (ovulation bleeding is not abnormal), further investigation is mandatory. A biopsy curet has its place in infertility studies, but certainly does not replace a D & C.

Biopsy—The same question arises here as with breast lesions: When should one biopsy?

Biopsy for conclusion of diagnosis should be done for such typical lesions as (1) the cauliflower, exophilic type; (2) the punched-out ulcer with firm edges that bleeds easily, and (3) the craterous, foul-smelling lesion that has replaced the cervix.

All these are clinically recognizable. A small piece from the edge of any will cinch the diagnosis.

TeLinde describes a suspicious lesion as follows:

1. Granulation tissue that bleeds on manipulation with cotton.

2. Small leukoplakic spots.

3. A polypoid area with a broad base.

4. Any hard area covered with epithelium.

5. A localized ulcer, even if small.

One more type should be added to the list:

6. Any simple erosion that does not heal after actual cauterization.

With a little experience, common velvety erosions and eversions are easily recognized. These need not be biopsied. When there is doubt or suspicion, always biopsy.

Schmitz has emphasized the importance of repeated biopsies if the lesion does not heal promptly.

The punch biopsy can be used as an office procedure because it is painless and controls bleeding; however, if possible, a wedge taken with the scalpel is cleaner and more accurate. A biopsy taken with a cautery knife is of little value to the pathologist. After biopsy, only enough of the lesion should be cauterized to control the bleeding. The biopsy specimen is taken at the junction of stratified and columnar epithelium or at the edge of the lesion.

Schiller's test—In detecting suspicious lesions, Schiller's test may be of help, but it is not diagnostic. The technic is to paint the cervix with Lugol's solution. The normal epithelium stains mahogany brown because the glycogen in the normal cells takes up the iodine. Carcinomatous areas do not absorb the iodine and therefore are light colored. Unfortunately, some erosions (columnar cells) and tight epithelium over tense nabothian cysts also do not take up the iodine.

Vaginal smears—Papanicolaou introduced a vaginal and cervical smear method for diagnosis of genital carcinoma in 1928. Consider-

able literature has been produced since that time concerning the true values of his technic. It can be said that the method is definitely helpful in diagnosis, particularly in the early cases before the physician can detect the presence of carcinoma.

The technic consists of drawing secretion from the posterior fornix and applying the secretion on a slide. It is spread evenly and then fixed in a solution made up of equal parts of 95 per cent alcohol and ether. A special method of staining is used. Training is necessary to evaluate the cytology.

Such benign conditions as some erosions, recent hormone therapy, and recent surgery may give false positive reactions. Carcinoma in other parts, such as bone, tube or rectum, can cause positive results.

Ayre's wooden spatula method, obtaining cells directly from the cervical os, is more accurate. The chief disadvantages are the time required for proper study of each slide and the need for an experienced cytologist.

A positive report demands a careful search by such sure methods of diagnosis as surgical biopsy, repeated if necessary, and/or D & C.

Incidence—Cancer of the cervix makes up 90 per cent of all uterine cancers. About 93 per cent of cancers of the cervix are squamous cell, while 7 per cent are adenocarcinoma. Cancer of the cervix occurs in about 0.4 per cent of all female hospital admissions. The condition is rare among Jewish women.

Carcinoma in Situ

No presentation on the care of the cervix is complete without at least a discussion of carcinoma *in situ*. The condition is also called intraepithelial or noninvasive carcinoma or Bowen's disease. TeLinde and Galvin of Johns Hopkins published their interesting work on this subject in January 1949.

Pathologically, the full thickness normally occupied by stratified epithelia is replaced by malignant basal cells. The cervical glands may be invaded and if so there is complete destruction of columnar epithelium. However, subepithelial structures are not invaded.

In order to complete this diagnosis, the entire cervix must be studied serially by the pathologist. There are now many cases of metastatic carcinoma of the cervix in which a single biopsy will show no invasion. Further biopsies in these instances would have shown the invasion. The treatment is radically different depending on whether there is invasion; therefore, it is of utmost importance to determine this fact beforehand. A true carcinoma *in situ* may appear dormant even under observation for many years. It is advisable, however, that the pathologist have the entire cervix before this diagnosis is acceptable. Most observers now report that with careful serial sectioning of the entire cervix, some points of invasion will frequently be found.

Clinical Classification

Broders of the Mayo Clinic has classified the grading of the tumor on cell morphology, which is in a general way accepted. Up to 25 per cent of cells with mitosis make up grade 1; 25 to 50 per cent, grade 2, and so forth. Other pathologists object, because the same tumor will show different grades in different areas. Generally speaking, the higher the grade of malignancy, the more rapidly growing and radiosensitive the tumor is and the poorer the prognosis.

The extent of the growth is the most valuable aid in prognosis. There are certain innate factors, such as host resistance and inherent tumor character, that make this tumor somewhat unpredictable. It is necessary, however, to have some common denominator in order to evaluate the various types of treatment. The League of Nations' classification of cervical carcinoma is the most uniform and generally accepted:

Stage I—Limited to the cervix.

Stage II—Limited to cervix and adjacent vagina. Parametrium may be involved slightly, but there is definite uterine mobility.

Stage III—Parametrium involved, with either partial or complete fixation.

Stage IV—Massive, hopeless. The parametrium is involved with metastasis to viscera or distant parts.

Stage 0—Now accepted in League of Nations' classification is stage 0 to designate carcinoma *in situ*.

Treatment of Carcinoma of the Cervix

Some of the older surgeons, such as Schauta and Wertheim, attempted surgical treatment of cancer of the cervix, but the high surgical mortality and poor salvage rates caused them to discard this method. They recommended radiation as standard treatment.

It is only natural that some of our present day surgeons would revive a surgical approach because of the improvement in technic and the advent of antibiotics, safe anesthesia and blood transfusions. We must wait for further reports from specially trained gynecologic surgeons before the proper evaluation of this procedure can be made. However, up to the present time, when large groups of cases are carefully reviewed, final analysis definitely demonstrates that, today, thorough and properly applied radium and adequate deep roentgen rays are still the treatments of choice.

Schmitz of Chicago probably has given us a good practical approach—all patients with carcinoma of the cervix are subjected to radiation therapy. Those who do not respond well are then subjected to surgery, depending on the risk, stage, and so on.

Roentgen treatment—X-ray therapy should be administered before radium application because of the following advantages:

1. Lymphatics are sealed and cancer cells theoretically destroyed before any manipulation coincidental to application of radium.

2. Infection accompanying the growth is brought under control. When radium is given first, many severe inflammatory reactions develop which prohibit the administration of the full dose of therapy.

3. An enlarged uterus or tumor mass involutes, making the radium more effective and application more accurate.

It is not within the scope of this presentation to describe in detail the technics of roentgen therapy; that is the responsibility of the roentgenologist. In general, he will direct the rays through several portals in order to get the maximum effect on the cervix and parametrium, as well as to attack other areas to be described.

The order of attack is as follows:

1. The local site is generally the first to be treated. Even when a large cauliflower growth is present, the center is treated just as with the ulcerating type. Growth of the exophilic tumor is from the center; it will melt down easily when treated at its source.

2. The parametrium and nodes.

3. The iliac nodes.

4. The secondary group of nodes—sacral, aortic and obturator.

5. Upper one-third of the vagina, including the vaginal lymphatics.

Radium treatment—Immediately after termination of the x-ray therapy, radium treatments should begin. A general plan, applicable to most cases, is administration of 5500 mg. hours through 5 portals. McKelvey, who has had outstanding results, uses the single dose method, while the Mayo group prefers the divided method. The total dosage with either procedure is quite similar, however.

We use the divided dose method:

First application: 2000 mg. hours in the uterine cavity with a 1 mm. platinum capsule filter covered with a thin rubber protector.

Second application: 1000 mg. hours in the cervical canal with a 1 mm. platinum capsule filter.

Third application: 1000 mg. hours to cervical portio with 1 mm. platinum and 1 cm. rubber.

Fourth application: 750 mg. hours to each lateral fornix, using the same filter as in the third application.

Individual circumstances may make it necessary to combine applications or to adjust dosage.

It is probably unnecessary to mention that the bowel should be well emptied prior to the treatment. The bladder and rectum should be packed as far away as possible to reduce to a minimum the effects of the rays on these organs.

The firm packing also serves to hold the radium securely in its proper position. McKelvey soaks the packing in some mild antiseptic solution. Continuous drainage of the bladder with an indwelling catheter is used until the radium is removed.

McKelvey hospitalizes all patients during the entire course of x-ray and radium therapy, stressing the importance of good diet and hygiene at this time. This is not feasible in private practice. We treat all our cases on an outpatient basis without untoward effects.

Prognosis

Cures are based on 5 year survival rates and are expressed as absolute or relative.

Absolute refers to the total number of patients living and free of any evidence of cancer 5 years after treatment against the total number applying for treatment. Relative survival rate refers only to those who were actually treated and survived 5 years without evidence of any recurrence.

It should be realized that survival rates closely parallel the meticulousness with which adequate treatment is carried out. Carcinoma of the cervix should be treated either thoroughly and adequately with known dosages of radium and x-ray or not at all. Haphazard treatment of this condition with a single piece of radium whose dose is outlined by a mail-order house should be discouraged. The lesion can be properly treated by those interested if they know the treatment outlined.

The mortality rate is less than 1 per cent. The survival rate is, generally, 75 per cent in stages I and II, 40 per cent in stage III, and 10 per cent in stage IV.

Cytologic studies do not particularly aid in predicting the response to treatment. The stages of the disease and radiation response definitely influence the outlook. Radiation response cannot be predicted.

Complications

Some of the side effects of therapy are as follows:

1. Enteritis, proctitis and cystitis in some degree are experienced by most patients, but usually clear up in 6 weeks. In a few patients, rectal stenosis may result some years later. On rare occasions a rectovaginal or vesicovaginal fistula may form. Surgery may be performed for these complications, but results are poor because of scarring and poor blood supply.

2. Anemia may occur. If pronounced or if the leukocyte count drops below 2000 per cubic millimeter, treatment should be postponed temporarily.

3. Ureteral obstruction should be recognized early and dilatations done. Genitourinary evaluation should be made prior to treatment, particularly in stages III and IV.

4. Vaginitis is usual and will often close the vagina into a nonfunctioning organ.

Noninvasive cancer—Treatment of noninvasive cancer is essentially conservative. Once a diagnosis is made by serially sectioning the cervix, treatment has been essentially completed. In other words, simple amputation of the cervix or total hysterectomy cures stage 0. Again one must be careful, however, not to depend on a single biopsy to complete the diagnosis of stage 0.

Carcinoma of the Cervix in Pregnancy

Treatment of carcinoma *in situ* in pregnancy is controversial—i.e., either conservative or radical. No less an authority than Greenhill suggests observation closely during and following the pregnancy, provided the lesion does not progress. Sometimes the cell structure occurring normally in pregnancy simulates that of a malignancy, and one must be careful to correlate the pathologic specimen with the clinical picture of the lesion itself.

A suggested outline for treatment of positive cancer of the cervix during pregnancy is as follows:

1. If the cancer is operable and child not viable, either surgery or radiation therapy.

2. If the cancer is operable and child viable, cesarean section followed by surgery or radiation.

3. If the cancer is inoperable and child not viable, radiation only.

4. If the cancer is inoperable and child viable, cesarean section followed by radiation.

Because of the high incidence of defective offspring, if the patient's religion permits, the uterus should be emptied when radiation does not produce abortion.

SCIENTIFIC EXHIBIT

Modern Otorhinolaryngology

KENNETH M. DAY AND THOMAS B. McCOLLOUGH

Eye and Ear Hospital, Pittsburgh, Pennsylvania

ANTIBIOTICS have not solved all the problems of the otorhinolaryngologist, and the specialty did no more disintegrate with the advent of antibiotics than did urology with the discovery of sulfanilamide and its related compounds. The scope of otorhinolaryngology has increased and the results have improved through (1) the discovery of antibiotics, (2) the recognition of the role of allergy in diseases of the ear, nose and throat, (3) the recognition of the need for rehabilitation of the deaf, (4) improved technics for plastic reconstructive surgery and (5) the recognition that malignant tumors about the head and neck can be treated with good results.

SOUND BEGINNING

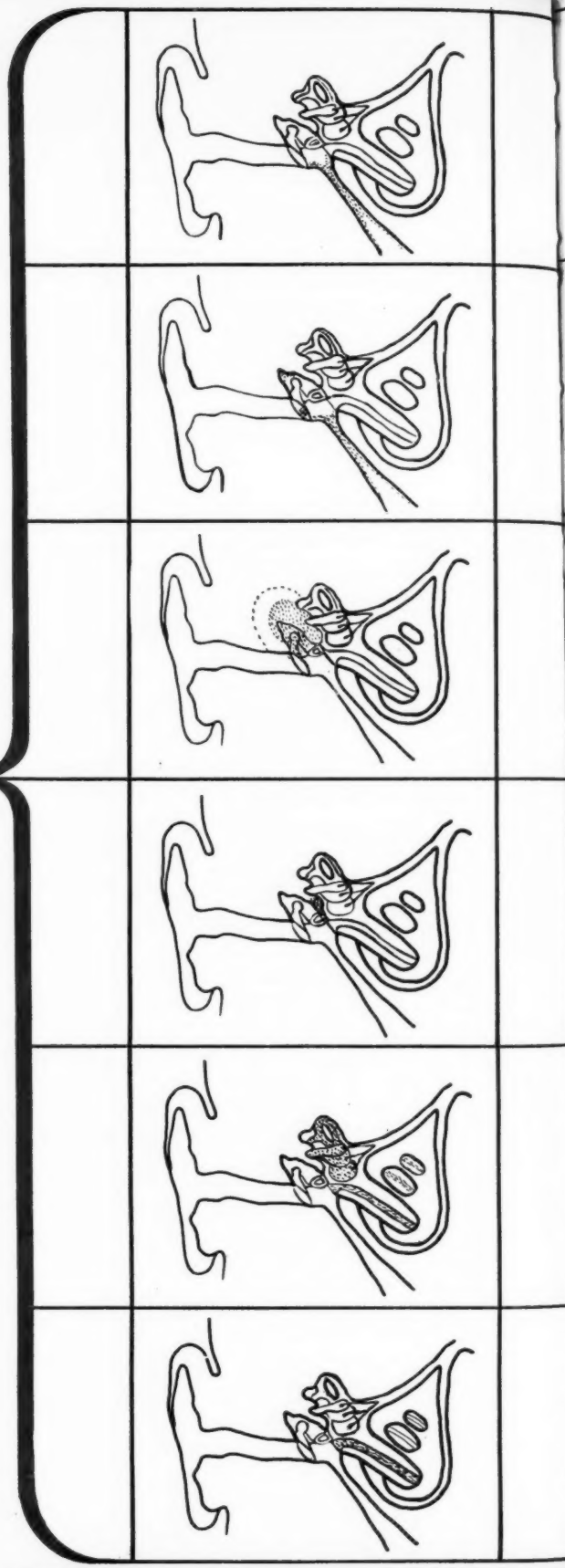
To relieve the busy practitioner of this important and time-consuming problem, a speech correction and hearing center with training facilities was installed as a central hospital agency to serve the community. Infants below 1 year of age, school children, adults and elderly individuals with problems of senility are some of the wide range of hearing problems handled by the Audiology Center. The audiologist also furnishes information which may be of diagnostic value to the otologist in treatment and surgery.

From an exhibit at the annual meeting of the American Medical Association in Chicago, 1952.

Patient of Department of Audiology of Eye and Ear Hospital.

Miss McKinney of the Department of Audiology of the Eye and Ear Hospital using visual means such as picture books and the shape of the mouth together with a working speaker (in toy telephone) to aid youngsters in association of sound and object, though deaf or partially so.

HEARING LOSS



Chronic Secretory Otitis Media—Not a new disease but an old condition with a new name. Characterized by a sterile transudation in the middle ear. Sixty-nine per cent of cases are in children less than 10 years of age. Deafness may be the only symptom. The child may not be backward—he may have hearing loss. The condition is not affected by the antibiotics. In 85 per cent of cases there is associated allergy. Watch for it in the child with frequent colds, running nose and earaches. The condition is reversible; the sequelae are not.

The unwanted child, dumb or "moronic" because of hearing loss. A curable but often unrecognized hearing loss resulting from fluid in the middle ear.

Chronic Suppurative Otitis Media—Persistent discharge may be caused by an underlying allergy. Many cases with persistent discharge from a central perforation (so-called simple otitis media with tubal discharge) were found to have an associated allergy. Food allergies are not uncommon in these cases. Milk is a common offender in children. The antibiotics will not produce a dry ear if the underlying cause is an allergy. Irreversible hearing loss can result from persistent discharge. Chronic suppurative mastoiditis may result from improper treatment. Practical hearing may be preserved by early conservative treatment or by modified radical mastoidectomy. Following complete radical mastoidectomy, practical hearing is rare.

Hearing loss resulting from an aural polyp. Neglected care of a chronically discharging ear.

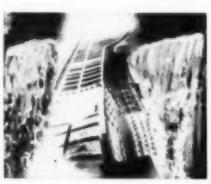
Chronic Mastoiditis with Cholesteatoma—Has been observed to be a complication of improperly treated chronic secretory otitis media. The negative pressure created in the mastoid attic and middle ear cavities by eustachian tubal block has resulted in an inward rupture of shrapnels and subsequent attic cholesteatoma. This phenomenon can take place in the absence of infection. This can be one of the reasons that the number of mastoids with cholesteatoma has not changed with the advent of the antibiotics. This is a potentially dangerous type of ear condition but early recognition and treatment may result in a considerable saving of hearing.

Facial paralysis—beauty destroyed by neglected care of an infected ear.

Otosclerosis—A prevalent type of progressive conductive deafness without apparent disease. This condition may occur at any age, but the common age of onset is the late teens or early twenties. The diagnosis was proved at surgery in a 7 year old child. Fenestration offers relief in a high percentage of suitable cases. The operation is not indicated in those cases with severe secondary nerve damage. Almost any type of hearing aid is helpful in those cases not suitable for surgery. Total deafness is rare.

The physical dangers of hearing loss as represented by the man walking in front of the automobile which he did not hear approaching.

Menière's Disease—Not a trash pile of symptoms but a definite clinical entity characterized by fluctuating nerve deafness, low-pitched tinnitus, violent and sudden attacks of true vertigo, distortion of sound and sensitivity to loud sound. Menière's disease can be diagnosed before the onset of vertigo. In a series of 220 cases 45 were diagnosed without vertigo and 83 patients gave a history of deafness, tinnitus and distortion of sound in the involved ear before the onset of vertigo. Patients treated before the onset of vertigo showed a more favorable response than those treated after vertigo was established. Destruction of the labyrinth has been uniformly successful in controlling unilateral cases in which there was no response to treatment or in which the vertigo was too severe to permit treatment. To date there have been no deaths resulting from this procedure.



A world of comparisons and distortion created by uniting the structure of a skyscraper and Niagara Falls. So is the spinning world of the individual afflicted with the vertigo of Ménière's disease.

Traumatic Deafness—It is not necessary to make boilers to get boilermakers' deafness. Traumatic deafness is characterized by a high tone hearing loss gradually progressing to involve the speech range. This is the patient who says, "I can hear but I can't understand," and who is sometimes accused of hearing only what he wants to hear. This condition does not respond to medical treatment and only a few such persons can wear hearing aids. They do not want loudness; they want clarity. A hearing aid gives only loudness.

A new problem in a mechanical and industrial age—traumatic hearing loss. Much is to be learned and much to be done to control damaging noise and protect this mass of individuals.

CORRECTIVE NASAL SURGERY

RHINOSINUSITIS AND THE STUFFY NOSE

The reaction of the nose to any stimulus is the same—congestion and increased secretion. The degree of reaction varies and depends on the strength of the stimulus and the nasal threshold or susceptibility to that stimulus. Nasal pathology depends on the degree of reaction and the duration of the stimulus. It should be remembered that the reaction is reversible with the removal of the stimulus unless the condition has progressed to the point of hyperplasia and fibrosis. Then the point of irreversibility has been reached and surgery becomes indicated. Early and adequate treatment is the best and only prophylaxis.

REMOVAL OF STIMULUS

Cleaner atmosphere

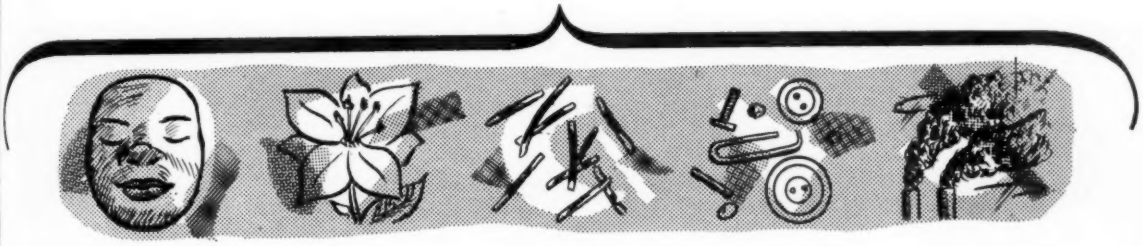
Antibiotics

Allergy treatment

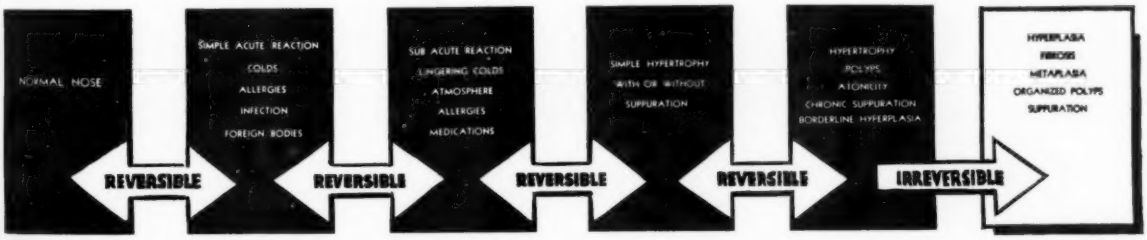
Submucous resection was described by Ingalls of Chicago in 1882 and was improved by Freer in 1902. It has remained the same for 50 years. In many cases this operation is inadequate. Submucous reconstruction is the application of rhinoplastic procedures for correction of external nasal and septal deformities that interfere with normal respiratory function.

Stressing functional reconstructive measures for proper physiologic function in contradistinction to cosmetic improvement.

ALL THESE MAY CAUSE A STUFFY NOSE



Anatomic abnormalities | *Allergies* | *Bacteria* | *Foreign bodies* | *Smoke*



SURGERY

Stuffy nose—the how, when and what to do about rhinosinusitis. Etiology, pathologic process and treatment of a large group of your practice.

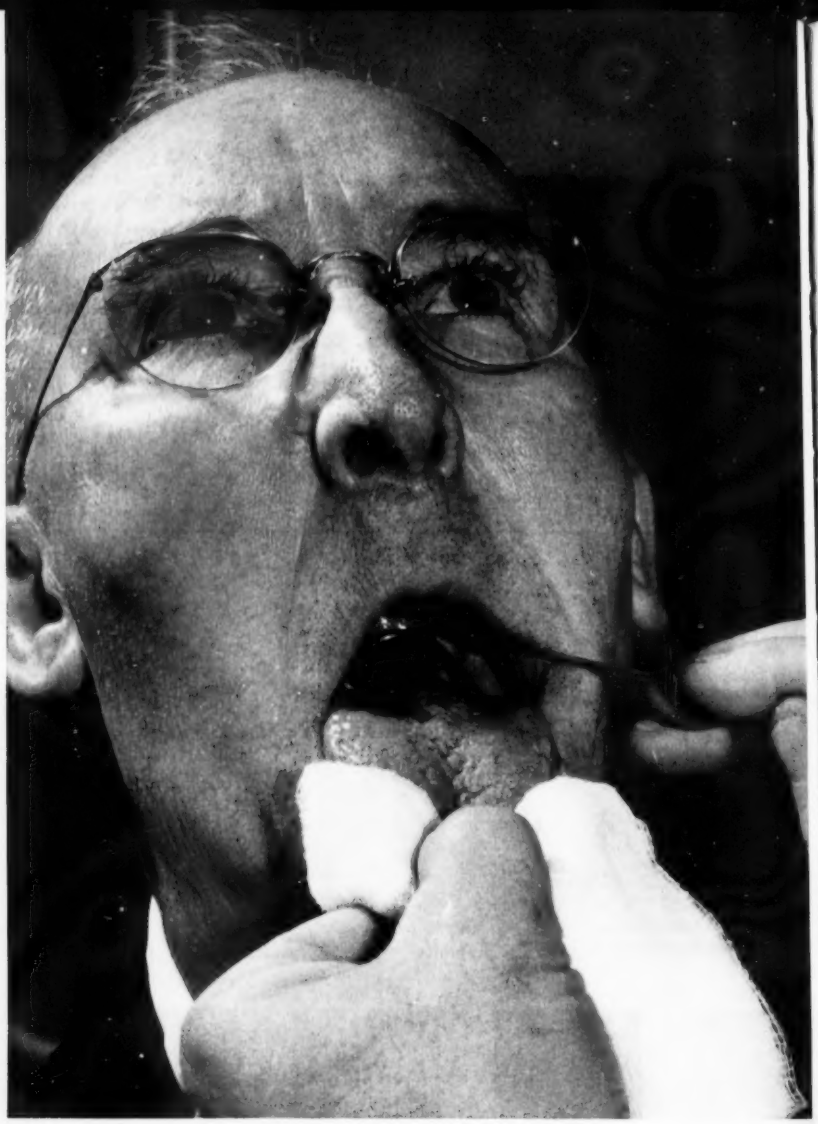
Almost any physician can afford one

It's not a very heavy instrument

You needn't be a magician to use it

Only rarely does the patient snap

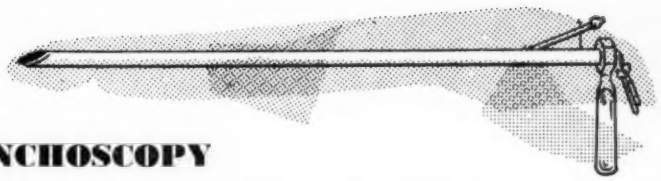
IT'S DONE WITH A MIRROR



LARYNGOSCOPY

The laryngeal mirror is an ever increasing and important diagnostic aid in this period of cancer consciousness. Its use will clarify the frequent diagnosis of "laryngitis" in persistent hoarseness.

Laryngeal examination is indicated in every patient with hoarseness of two weeks' duration. Eighty-five to 95 per cent of persons with laryngeal cancer can be saved if diagnosis is made early. Cure rate today is about 45 per cent due to late diagnosis. Laryngeal examination with a mirror is an office procedure, but is not being done as often or as early as it should be. It is essential to proper diagnosis of hoarseness, hemoptysis, cough and dysphagia. Laryngoscopy should be done in every patient before diagnosis of chronic laryngitis is made. Laryngoscopy is essential in diseases of the lower pharynx. All is not asthma that wheezes—remember laryngoscopy.



BRONCHOSCOPY

The necessity for bronchoscopy is increasing because lung cancer is five times as frequent as it was 25 years ago. Bronchoscopy is the only hope of saving life in bronchogenic carcinoma of the lung. Bronchogenic carcinoma is second only to gastric cancer as the cause of cancer deaths in men. Early diagnosis by bronchoscopy is of utmost importance because only 10 per cent of the patients present themselves for treatment while the carcinoma is confined to the lung. The average physician may delay seven months in establishing the proper diagnosis, thereby permitting the carcinoma to become inoperable.

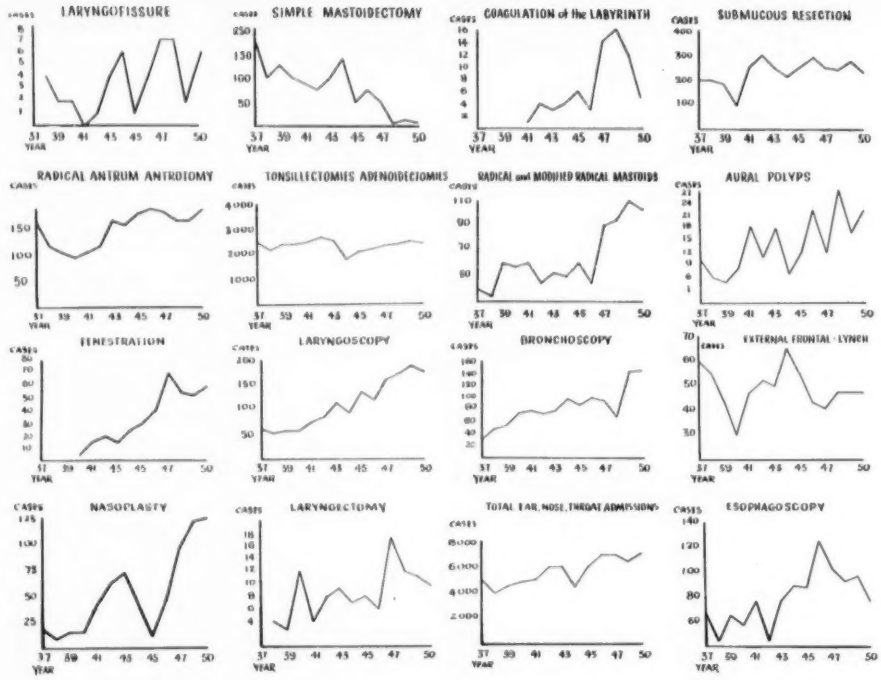
Bronchoscopy is essential in every patient more than 40 years of age with unexplained thoracic disorder. The physician may assume the presence of bronchogenic carcinoma in every man more than 40 with lung symptoms until proved otherwise.

Bronchoscopy is indicated for cough, hemoptysis, low grade fever, chest pain, dyspnea and wheezing. Bronchoscopy is the greatest single aid in the diagnosis of pulmonary carcinoma. The bronchoscopist can directly visualize the lesion, obtain a biopsy specimen and collect bronchial secretions for cytologic study.

Bronchoscopic aspiration has shown cancer cells in 40 per cent of 54 proved cases of lung carcinoma. Other pathologic processes affecting the lung requiring bronchoscopic examination are benign tumors, foreign bodies, bronchiectasis, lung abscess, laryngotracheobronchitis, and bronchial secretions in asthma.

ESOPHAGOSCOPY

Esophagoscopy is essential for early diagnosis of carcinoma of the esophagus and is the most helpful aid in saving the patient with this disease. Esophagoscopy is indicated first and most commonly in the presence of dysphagia. Other indications are substernal pain, loss of weight with esophageal obstruction, hoarseness and brassy cough. Other esophageal abnormalities requiring esophagoscopic examinations are diverticulum, cardiospasm, ulcer, stricture, spasm, benign tumors and foreign body.



Graphic Records of Surgical Procedures, 1935 to 1950, at the Eye and Ear Hospital, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania.

Laryngofissure—Suitable cases for this procedure are infrequent. Hoarseness is not a disturbing symptom. Diagnosis is delayed because (1) patient fails to seek medical advice; (2) physician fails to do a laryngeal examination.

Simple Mastoidectomy—A conquered disease as the result of proper antibiotic therapy. It is successful because the patient with earache consults the doctor early.

Coagulation of the Labyrinth—An improved surgical procedure for rehabilitation of the individual with aural vertigo. The decline may be associated with a better understanding of the underlying pathologic process and of the physiology, with improved medical therapy as a result.

Submucous Resection—A persistent entity with but one answer for relief—surgical correction.

Caldwell-Luc—Improved results with antibiotic therapy and allergic management, but still a surgical necessity.

Tonsillectomy—The necessity for surgery is unchanged by antibiotics.

Radical and Modified Radical Mastoidectomy—Increase accounted for by improved results with better surgical procedures and antibiotics. There is also the question of neglected cases of acute mastoiditis kept dangerously quiescent with antibiotics.

Fenestration—A new and improved procedure.

Endoscopy—Increased due to stress on diagnosis and therapy of malignancy.

External Frontoethmoidectomy—A relatively constant procedure uninfluenced in frequency by antibiotics because patients do not seek medical care early.

Nasoplasty—Increased due to stress on corrective nasal function including the lateral nasal wall.

Laryngectomy—Increased due to stress on diagnosis of malignancy.

Ear, Nose and Throat Admissions—A gradual but not remarkable increase, due to limited facilities.

Esophagoscopy—Increasing as a result of cancer education. The late decline is due to the affiliation of the Thoracic Surgery Department.

Pediatrics IN GENERAL PRACTICE

For general practitioners, who handle more than 85 per cent of all pediatric care, POSTGRADUATE MEDICINE *here presents authoritative, up-to-date summaries by specialists in pediatric problems.*

The Role of Potassium in Fluid Therapy

ROBERT E. COOKE*

Yale University School of Medicine, New Haven, Connecticut

THE use of potassium in fluid therapy must be planned according to the same logical principles as are applied to use of water and other electrolytes.[1]

ROBERT E. COOKE

The first phase of fluid therapy is concerned with correction of any pre-existing disturbances in body composition; this may be termed deficit therapy.

The other two principles of therapy are concerned with the prevention of disturbances in body composition and have been described as maintenance therapy and the concomitant replacement of abnormal losses. Maintenance therapy is essentially parenteral nutrition and consists of the supply of water, electrolytes, protein and calories as they are lost from the body in usual existence. The concomitant replacement of abnormal losses, as the term implies, consists of meeting extraordinary losses such as those resulting from vomiting, gastric drainage, etc.

Any logical analysis of potassium therapy must be considered according to such an outline.

Deficit Therapy

Deficits of potassium have been described in a myriad of clinical states.[2] Table 1 summarizes these conditions. If intake is inadequate or losses excessive, potassium deficiency will result. In this connection it is important to realize that the administration of saline and glucose increases rather than decreases the likelihood of potassium deficiency since renal losses of potassium are increased in this way. In addition, shifts of potassium from extracellular fluid to intracellular fluid may occur and lead to severe hypopotassemia.

Detection of Potassium Deficiency

The presence of potassium deficiency cannot always be detected by usual laboratory or clinical procedures.

The following laboratory and clinical signs of potassium deficiency are frequently absent

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TABLE 1

CLINICAL STATES COMPLICATED BY POTASSIUM DEFICIENCY

I. Inadequate intake
  a. Starvation
  b. Parenteral therapy with saline and glucose
II. Excessive losses
  a. Gastrointestinal
    Pyloric stenosis, pernicious vomiting; salivary, gastric, intestinal, biliary, pancreatic drainage; diarrhea, colitis, sprue; laxative habit; resin therapy
  b. Urine
    1. Intrinsic disease—chronic nephritis, lower nephron nephrosis (recovery phase)
    2. Extrinsic influences—alkalosis, diabetic acidosis; mercurial diuretics
      Hyperadrenalism
        a. Endogenous—Cushing's, stress
        b. Exogenous—ACTH, cortisone, DOCA®
III. Redistribution
    Diabetic ketosis (therapy)
    Familial periodic paralysis

in patients who have been shown to be potassium-deficient by recovery balance technics.

1. Low serum potassium—especially at the beginning of therapy.
2. Metabolic alkalosis.
3. Abnormal electrocardiogram—low T waves, prolonged QT interval.
4. Skeletal muscle weakness.
5. Smooth muscle atony such as intestinal ileus.
6. Cardiac muscle dysfunction.

For example, potassium deficiency is unquestionably present and can be demonstrated by balance technic in protracted vomiting, diarrhea, etc., even though all the classic signs of potassium deficiency are absent.[3]

Thus, the presence of potassium deficiency can and must be recognized by the preceding history, and overt signs of deficiency need not be present before potassium therapy is initiated. If characteristic laboratory or clinical signs are noted, the suspicion of potassium deficiency is confirmed.

The magnitude of the deficit of potassium in the common pediatric conditions has been determined by recovery balance technic, by balances performed during the development of experimental deficiency and by radioisotope dilution technics. Table 2 indicates the results of such studies in infants, children and adults. The deficits of potassium in adults per kilogram of ideal body weight* are of the same order of magnitude as in infants as indicated by the findings of Atchley, et al.[7] and Butler, et al.[8]

Replacement of Potassium Deficit

The replacement of the deficit of potassium is carried out in a similar way in these conditions. The accompanying Therapy Charts represent the program used by the author.

In diarrhea, Darrow's potassium lactate solution (K N L) is used as the source of potassium since metabolic acidosis and hyperchloremia are usually present. In pyloric stenosis potassium is administered as the chloride, since metabolic alkalosis and hypo-

*As given by insurance tables.

TABLE 2

POTASSIUM DEFICIT

DISEASE	DEFICIT *mEq./Kg.*	TECHNIC OF DETERMINATION	AUTHOR
Diarrhea	8-12	Recovery balance	Darrow, et al.[3]
Pyloric stenosis	10-14	Recovery balance	Danowski, et al.[4]
Diabetic ketosis	6	Recovery balance	Darrow and Pratt[5]
	4-6	Recovery balance	Danowski, et al.[6]
	6	Development balance	Atchley, et al.[7]
	6	Development balance	Butler, et al.[8]

THERAPY CHART I

DIARRHEA
INFANT
Moderately Severe Dehydration

Serum
CO_2— 12 mm./L.
Cl —110 mm./L.

FLUID	CC./KG.	TIME (Hours)	SITE	ELECTROLYTE (MM./KG.)				PURPOSE
				Na	*K*	*Cl*	HCO_3	
Ringer lactate	10	0-½	I.V.	1.3		1.1	0.3	Expand B.V.
Whole blood	10	½-1½	I.V.	not considered in deficit				Correct shock
10% invert sugar in H_2O	40	1½-6	I.V.	0	0	0	0	Correct ketosis and H_2O deficit
K lactate	80	1-6	S.C.	9.6	2.8	8.2	4.2	Correct Na and Cl and part of K deficit
TOTALS	140			10.9	2.8	9.3	4.5	

Proceed with Maintenance Therapy

chloremia are usually present. In diabetic ketosis potassium is administered as the phosphate, since hypophosphatemia usually develops in this condition.

The quantity of each of these solutions administered to a large child or adult is reduced approximately one-third for the same clinical degree of dehydration as in the infant.

In *all* cases, replacement of the deficit of potassium must be preceded by the administration of water and extracellular electrolytes (Ringer lactate or saline) to correct extracellular dehydration, shock and anoxia and improve renal function.

Extracellular electrolytes (sodium and chlorine) may be given with relative impunity. Intracellular electrolytes (potassium, magnesium and phosphorus) must be given with caution and only after some improvement in urine formation has been effected. Only part of the deficit of potassium (2 to 3 mEq. per kilogram) is replaced rapidly (4 to 6 hours). The balance of the deficit (4 to 10 mEq. per kilogram) is restored gradually during adequate maintenance therapy.

The usual practice on our service is to administer potassium replacement solutions by hypodermoclysis over 4 to 6 hours. This procedure is considered of greater safety than intravenous administration, since accidental

THERAPY CHART II

PYLORIC STENOSIS
INFANT
Moderately Severe Dehydration

Serum
CO_2—40 mm./L.
Cl —80 mm./L.

FLUID	CC./KG.	TIME (Hours)	SITE	ELECTROLYTE (MM./KG.)				PURPOSE
				Na	*K*	*Cl*	HCO_3	
Isotonic saline	20	0-1	I.V.	3.0	0	3.0	0	Expand B.V.
Blood	10	1-2	I.V.	not considered in deficit				Correct shock
Isotonic NaCl	40	1½-7	S.C.	6.0	0	6.0	0	Correct Na, Cl and part K deficit
Isotonic KCl	20	1½-7	S.C.	0	3.0	3.0	0	
5% glucose in saline	30	2-5	I.V.	4.5		4.5		Correct ketosis and Na and Cl deficit
10% invert sugar in H_2O	20	5-7	I.V.	0	0	0	0	Correct ketosis and water deficit
TOTALS	140			13.5	3.0	16.5	0	

Proceed with Maintenance Therapy

THERAPY CHART III

DIABETIC KETOSIS
INFANT
Moderately Severe Dehydration

Serum	
CO_2	5 mm./L.
Cl	105 mm./L.
Na	135 mm./L.

FLUID	CC./KG.	TIME (*Hours*)	SITE	ELECTROLYTE (MM./KG.)					PURPOSE
				Na	*K*	*Cl*	HCO_3	PO_4	
Ringer lactate	20	0-1	I.V.	2.6	0.1	2.2	0.6	0	Expand B.V.
M/6 Na lactate	15	1-2	I.V.	2.4			2.4		Correct *p*H
Ringer lactate	40	2-7	S.C.	5.2	0.2	4.4	1.2		Correct Na, K, Cl and P deficit
*K phosphate solution	40				2.4			1.3	
10% invert sugar in H_2O	30	2-7	I.V.	0	0	0	0	0	Prevent hypoglycemia, correct H_2O deficit *s* salt
TOTALS	145			10.2	2.7	6.6	4.1	1.3	

*5% glucose — 500
K_2HPO_4 concentrate — 10
K — 60 mm./L.
K_2HPO_4 — 26.4 mm./L.
$KHPO_4$ — 7.4 mm./L.
P — 33.8 mm./L.

Proceed with Maintenance Therapy

potassium intoxication may result from rapid intravenous infusion of solutions of high potassium concentration (>30 mEq. per liter) at times when there is a shortage of nursing personnel.

Maintenance Potassium Therapy

The prophylactic use of potassium is of equally great importance as deficit therapy, but it is frequently neglected in routine parenteral therapy. Unless potassium is administered as losses occur in usual existence, alterations in body composition and function will result. Table 3 lists some functions known to be dependent on presence of potassium.

The failure to administer potassium in maintenance therapy may be likened quite accurately to the failure to use vitamin D in the prevention of rickets. Vitamin D is not withheld until flagrant rickets is present, nor should potassium be withheld until hypopotassemia develops.

The requirement of potassium for maintenance is based on the same principles as the requirements for water and sodium. The supply of potassium must meet the usual losses of potassium. These losses are relatively independent of the size or weight of the patient but are proportional to the rate of turnover.[2] Therefore, maintenance dosage and requirements are expressed per hundred calories metabolized.

Table 4 presents the usual losses of potassium. Urine losses may be considerably greater if large quantities of sodium chloride or sodium bicarbonate are given.

TABLE 3

ACTION OF POTASSIUM

1. Nerve—repolarization
2. Muscle—skeletal, smooth, cardiac
3. Glands—gastric
4. Kidney—glomerular filtration rate; chloride conservation; bicarbonate excretion
5. Liver—carbohydrate utilization; glycogen synthesis; phosphorylation
6. Tissue enzymes—cholinesterase inhibition; choline acetylase acceleration; protein synthesis acceleration

TABLE 4

USUAL POTASSIUM LOSSES
(MEQ. PER HUNDRED CALORIES METABOLIZED)

SITE	MINIMUM	USUAL
Skin	0.1	0.2
Stool	0.1	0.3
Urine	0.2+	1.0-5.0
TOTAL	0.4+	1.5-5.5

THERAPY CHART IV

USUAL DAILY MAINTENANCE

FLUID	CC./100 CALORIES METABOLIZED	TIME (Hours)	SITE	ELECTROLYTE (MM./100 CALORIES METABOLIZED)				
				Na	*K*	*Cl*	*P*	HCO_3
Maintenance solution*	140	24	I.V.	3.2	2.5	2.5	1.1	1.2

*CHO in H_2O .... 10 per cent**
K ..... 18 mm./L.
Na ..... 23 mm./L.
Cl ..... 18 mm./L.
P ..... 8 mm./L.

**$\bar{c}$ or $\bar{a}$ Amigen and/or alcohol.

The usual diet supplies approximately 5 mEq. of potassium per hundred calories metabolized. However, a somewhat lower intake of potassium (2.0 to 3.0 mEq. per hundred calories metabolized) is adequate, since nitrogen intake is usually limited during parenteral fluid therapy.

Such a system of calculation permits planning of therapy for individuals of all sizes and ages from prematurity to senility. Basal caloric turnover can be calculated readily from appropriate tables, and suitable increments for fever (1° F. = +8 per cent) and activity (usual bed activity = +10 to 20 per cent) may be added. The total number of calories metabolized by the usual afebrile adult approximates 2000 calories per day.

Therapy Chart IV presents the maintenance solution used by the author. At the present time it is compounded from Ringer lactate, potassium chloride concentrate and 10 per cent invert sugar. Similar solutions should be commercially available in the near future.

Obviously if potassium excretion is limited as in oliguria, the use of such a maintenance solution is contraindicated, since urine losses constitute the bulk of the usual losses of potassium, sodium and water. A determination of serum potassium concentration or an electrocardiogram should be obtained at 3 day intervals during parenteral therapy in every case.

TABLE 5

ABNORMAL LOSSES OF POTASSIUM

SITE	CONCENTRATION OF K (*mEq./L.*)
Diarrheal stools	20 — 60
Gastric fluid	10 — 20
Intestinal fluid	10 — 15
Pancreatic fluid	10 — 15
Bile	10 — 15
Saliva	20 — 30
Sweat	10 — 15
Urine	10 — 100

Concomitant Replacement of Abnormal Losses

The final consideration in adequate parenteral therapy is the replacement of extraordinary losses as they occur. Table 5 presents the usual range of potassium concentration in most abnormal losses. Although adequate maintenance therapy provides some margin of safety to meet occasional small abnormal losses, it is essential to replace accurately more than minimal losses.

Volume for volume replacement of gastric or intestinal drainage with commercially prepared solutions has been described by Hurwitz, et al.[9] and Cooke and Crowley.[1] Such a system of replacement has definite advantages over the use of saline or glucose for replacement and is technically no more difficult or laborious to use.

Summary

Potassium has been demonstrated to be of fundamental importance in body function. Consequently not only must deficits of potassium be replaced but also the development of new deficits must be prevented by adequate maintenance therapy and abnormal loss replacement. In this way, optimal cell function may be attained.

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Effects of Cortisone and Corticotropin on Allergic Reactions

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Cortisone and corticotropin are relatively new entries in the field of therapeutics, but their advent has been most dramatic. They have been widely and successfully used in the treatment of allergic disease. Being hormones directly concerned with one of the great integrative systems of the body, these agents have actions which are far from simple and the avenues open to research are many. No attempt to review this voluminous literature will be made. Evans and Rackemann[1] have surveyed the literature concerning their use in allergy, and Thorn, et al.[2] have reviewed the whole scope of the adrenocortical steroids and corticotropin.

Effect on Antibodies

Two qualitative tests for the presence of antibodies concerned with allergic diseases have stood the test of time: (1) The scratch or intradermal skin tests with specific antigens can give information regarding cellular antibodies. (2) Passive transfer tests may provide data about circulating antibodies.

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Leith, Graham and Burrage[3] of this laboratory reviewed a group of patients with seasonal hay fever due to various pollens. Each had good-sized, immediate skin reactions to the offending pollen, and the serum of each patient produced positive passive transfer tests. Each patient had 20 mg. corticotropin intramuscularly every 6 hours for 8 doses. Skin tests were repeated, and blood was withdrawn for passive transfer tests 4 hours after the last injection of ACTH. In most patients the skin tests and passive transfer tests remained positive. Figures 1 and 2 show the skin tests and passive transfer tests both before and after ACTH. Corticotropin did not

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FIGURE 1

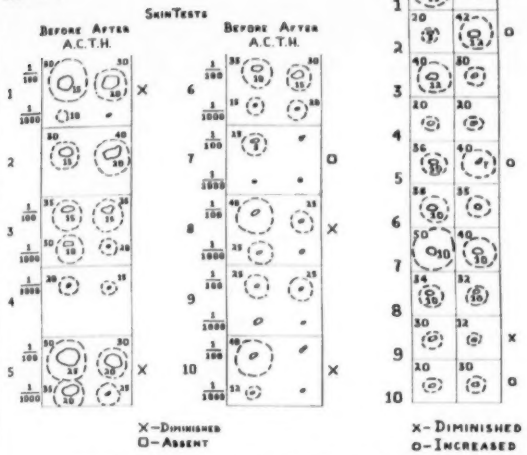
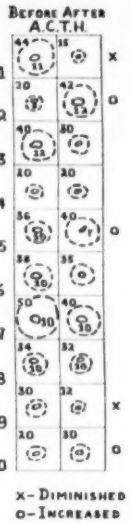


FIGURE 2 *(right)*



(Figures 1 and 2 from Irwin, John W., Leith, W. and Graham, M. J.: The effect of ACTH on the immediate skin reaction and passive transfer test in man. J. Allergy 22:99-105, 1951. Reproduced courtesy The C. V. Mosby Company, publishers.)

completely destroy either cellular or circulating antibodies.

Effect on Small Blood Vessels

It is possible to study the blood vessels of the bulbar conjunctiva of a human patient by means of a stereoscopic microscope and reflected light as described by Knisely, et al.[4] Figure 3 visualizes this method. It is possible to determine to a limited degree the condition of the blood vessel walls and to study in more detail the intravascular cellular elements. To date our observations have been limited to patients with severe asthma before, during and after cortisone therapy. Initial studies in these patients indicate that arterioles constricted, venules dilated, and red blood cells formed into aggregates which were more predominant on the venous side during cortisone therapy. Figure 4 shows these aggregates in a small vein.

Use of Cortisone and Corticotropin in Allergic Disease

Accumulated evidence at this time fails to show that these hormones basically alter antibodies. They relieve the symptoms of allergic disease through mechanisms not as yet understood; clinical symptoms return after the administration of either hormone is stopped. It would, therefore, seem wise to keep the following principles in mind: Attempts should be made to ascertain the offending antigens and to separate the patient from them; if an antigen such as ragweed pollen can not be avoided, hyposensitization should be tried; in serum sickness and drug allergy, primary attention should focus on prevention.

The undesirable effects of these hormones are well known. To avoid serious difficulty in regard to fluid balance, all patients receiving these agents should be placed on low sodium diets, and blood electrolytes (sodium, potassium and chloride) should be checked periodically. Cortisone and corticotropin have been reported to have adverse effects in tuberculosis, to cause severe gastrointestinal bleeding in certain instances, to make diabetes more difficult to control, to precipitate neuropsychiatric crises, and to enhance thromboembolic disorders. A past or present history of any of the above diseases may well contraindicate the use of these hormones. Infectious diseases, with special emphasis on the possible acquisition or activation of tuberculosis, must never be forgotten before, during or after treatment with these agents. Cortisone and corticotropin may well delay longitudinal growth in children. Any child on maintenance

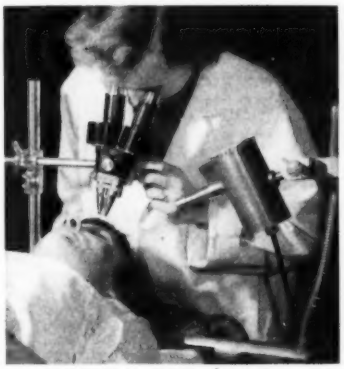
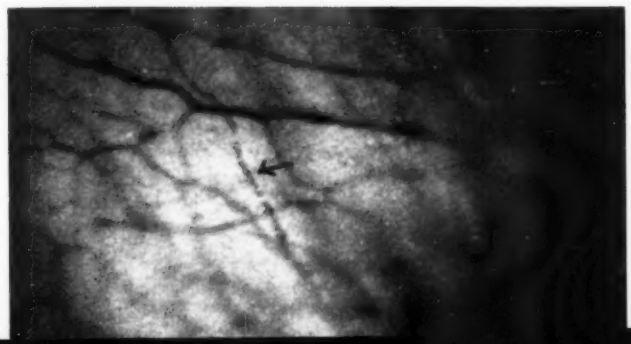


FIGURE 3

FIGURE 4 *(below)*



therapy should be checked accurately for longitudinal growth at regular intervals.

Asthma

Both cortisone and corticotropin are effective in relieving the symptoms of asthma, but in our hands cortisone has been the one of choice as its side reactions seem easier to avoid. Furthermore, cortisone is particularly suitable in children as it may be given orally. Candidates for this therapy come from the following 3 groups: (1) patients with status asthmaticus who have not responded to the usual forms of emergency therapy; (2) those seriously ill with pollen asthma who have previously been studied and frequently hyposensitized as well, but who have developed severe asthma unreactive to the usual means of therapy, and (3) a small group with intractable, constant asthma in whom study has failed to establish the offending antigens and in whom other therapy has failed.

In the first 2 groups, enough cortisone is given to free the child from asthma. The amount of cortisone required for this purpose does not seem to depend on the severity of symptoms nor on the body surface area. In children over 6 years of age, it is probably safe to prescribe 50 mg. every 6 hours for the first 24 hours and then give 25 mg. every 6 hours until the asthmatic symptoms subside. Gradually the dose is lowered. In pollen asthmatics it may be worth while to maintain the child through the pollen season. In such cases 12.5 to 25 mg. every 12 hours should be adequate. We have had no experience in treating infants in these first 2 groups. No children in the third group have been carried on maintenance therapy. However, we have maintained 14 adults almost free from asthma on daily doses of cortisone for periods varying from 1 to 2 years.[5] Table 1 shows the amount of cortisone and the length of time required to free each of these patients of

TABLE 1

CORTISONE COURSE (IN MILLIGRAMS) TO FREE PATIENTS OF ASTHMA

PATIENT	AGE	SEX	ROUTE	DAY														TOTAL (GRAMS)
				1st	2nd	3rd	4th	5th	6th	7th	8th	9th	10th	11th	12th	13th	14th	
N. Z.	51	F	Oral	100	200	300	200	250	300	300	225	200	150	75	75	75	75	2.525
E. M.	36	F	Oral	150	250	150	75											0.625
D. M.	57	M	Oral	150	250	200	200	150										0.950
E. W.	62	M	Oral	225	225	200	125	100										0.875
E. K.	42	F	Oral	225	275	150	100											0.750
M. S.	57	F	Oral	150	250	150	150	200	200	200	100	100						1.500
A. B.	57	F	I. M.	150	250	150	100											0.650
M. M.	61	F	I. M.	150	200	200	175	150										0.875
M. A.	42	F	I. M.	225	225	125	100	100	100	100	100							1.075
M. D.	55	F	I. M.	225	225	100	100	75										0.725
A. W.	55	F	I. M.	150	250	200	200	125	75	75	75							1.150
P. B.	69	M	I. M.	150	250	175	125	125	100	100								0.825
W. G. (a)	58	M	I. M.	150	300	200	200	150	100									1.100
W. G. (b)	59	M	I. M.	150	250	200	200	175	100	100	100	100	100					1.475
C. R.	58	M	I. M.	300	200	200	150	100	100	100	100							1.250

1. Daily doses divided into 4 (every 6 hours).
2. First day dose small as therapy started in mid-day.
3. W. G. (a), first course in 1951; W. G. (b), second course in 1952.

asthma. Figures 5, 6 and 7 record the daily maintenance dose of one of these patients through many months of therapy. Experience shows that each patient has his own maintenance level which must be found by trial and error.

A case report of one of the adults, maintained for months on cortisone, points out many of the problems.

Case Report

A 57 year old white woman, widowed, first developed asthma in 1921 when she was 25. No specific antigens were found at that time. Although the asthma was persistent, it could be controlled with various routine medications. Upper respiratory tract infections always increased her symptoms. During the winter of 1940-1941, bronchopneumonia developed with severe asthma, for which hospitalization was necessary. Following this illness, the asthma became increasingly difficult to control, until by May 1950 she was unable to work.

On November 23, 1950, status asthmaticus developed and the patient had to be rushed to the hospital. Aminophylline and glucose, given intravenously, along with epinephrine and general supportive measures, were ineffective. Four days later she started receiving corticotropin, 20 mg. intramuscularly every 8 hours, and after 48 hours she showed improvement. Gradually the dosage was decreased and on December 4, 1950, the hormone was discontinued. She went home almost free of asthma. Within the next 5 weeks her symptoms increased, however, and in mid-January 1951, she was again admitted to the hospital. After 5 days of therapy, other than hormonal, she was able to return home. In February 1951 she returned to the hospital in status asthmaticus. Treatment with corticotropin resulted in improvement and she was discharged on a dosage schedule of 10 mg. intramuscularly daily. In spite of this, she was in trouble again within 2 weeks. Her daily dose was slowly raised to 125 mg., but she failed to improve. She was readmitted to the hospital in mid-April 1951 and the ACTH was discontinued. Her course was again downhill and

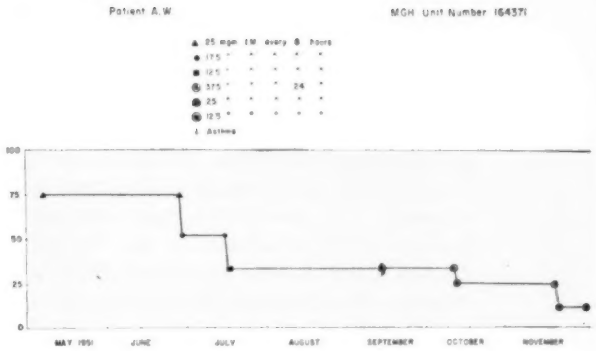


FIGURE 5

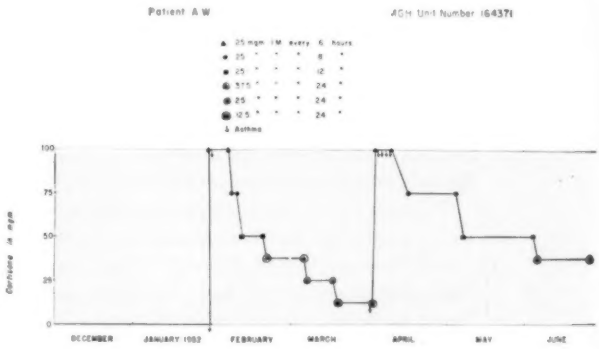


FIGURE 6

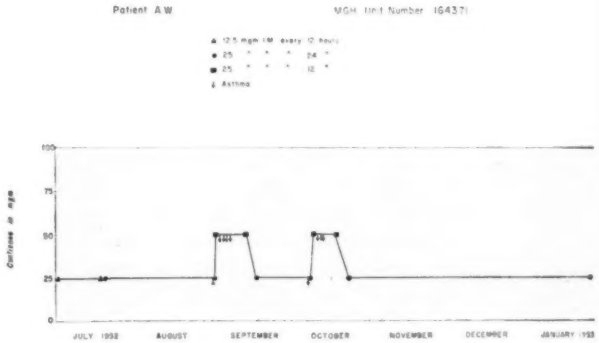


FIGURE 7

she returned to the hospital in May 1951 for yet another visit.

Physical examination revealed a tall woman who was apprehensive, wheezing audibly and struggling for breath. Her weight was 149

pounds and her blood pressure was 160/85. Routine tests showed no abnormalities. The anteroposterior diameter of the chest was increased, the sternum was prominent and there was marked hollowing of the jugular notch and supraclavicular fossa. The diaphragm was down with limited excursion. The lungs were hyper-resonant and there were inspiratory and expiratory musical rales and rhonchi in all fields. Vital capacity was 1 liter in 3 seconds. Roentgenographic and fluoroscopic studies of the chest showed marked limitation of movement of the diaphragm with flattening, bright lungs and emphysema.

A roentgenogram of the sinuses showed clouding of the right antrum. The circulating eosinophil count was 1,226 per cubic millimeter; blood chemistry values (per liter) were 141 mEq. sodium, 5 mEq. potassium, 104 mEq. chloride and 29 mEq. carbon dioxide. There was no reaction to multiple scratch and intradermal skin tests.

Figures 5 to 7 illustrate the patient's course while receiving cortisone, indicating that she could be maintained free of asthma with a daily injection of 25 mg. of cortisone. On April 4, 1953, she weighed 154 pounds, her blood pressure was 140/80 and her lungs were clear. The arterioles and venules of her bulbar conjunctiva contained red cell aggregates. On February 20, 1953, the blood chemistry values (per liter) were: 137 mEq. sodium, 3.7 mEq. potassium, 100 mEq. chloride and 30 mEq. carbon dioxide. Fasting blood sugar was 90 mg. per cent. Vital capacity was 3.8 liters in 3 seconds. Her glucose tolerance curve was normal in December 1952. She has done well and has not missed work. Her symptoms have been controlled, but she must continue on cortisone to be symptom-free.

Serum Disease

Diphtheria, tetanus and pneumonia antitoxins contain a foreign serum which, on injection after an incubation period of 1 to 17 days (usually averaging 7 to 10 days), may give rise to a symptom complex including urticaria, lymphadenopathy, fever, pain, swelling of joints, and nausea and vomiting. Albumin and red blood cells may appear in the urine. Von Pirquet and Schick[6] ascribed these symptoms to a reaction between diminishing amounts of the foreign serum (antigen) in the circulating blood and increasing amounts of antibody. These antibodies in the circulating blood were found by Longcope and Rackemann[7] to appear after the clinical manifestations began to clear.

Though toxoids and antibiotics have markedly reduced the use of antitoxins, serum disease from foreign serum in antitoxin still occurs. The symptoms usually quickly clear, and there is no need for cortisone or ACTH. In rare cases, however, the symptoms are very severe and persistent. Initially epinephrine can be used until cortisone or ACTH becomes effective. One to 3 short courses of either hormone have proved useful.

Once serum disease has developed from a foreign serum, the patient should never be given that serum again for he may respond violently and die within minutes. In such cases cortisone and ACTH are of no value for they do not act immediately. In other cases in which laryngeal edema and other symptoms are severe and persistent enough to warrant repeated epinephrine for control, cortisone or corticotropin can be very helpful. A 40 year old man who had previously responded to horse serum with serum sickness was injured. Again he received tetanus antitoxin. Angioneurotic edema and urticaria soon became so severe that he had to be hospitalized. The antihistamines were of little avail and epinephrine gave only transient and partial relief. He was given 75 mg. cortisone every 6 hours for 24 hours. During the next 48 hours he received 50 mg. every 6 hours, and improved markedly. The daily dose was gradually lowered to 50 mg. divided into 2 doses, with which he was maintained symptom-free for 10 days. Cortisone was then stopped, but his symptoms returned within 4 days. Again he was hospitalized, cortisone resumed and a maintenance daily dose re-established for 2 weeks before finally being discontinued. He remained symptom-free thereafter.

Drug Allergy

In recent years the appearance of toxoids

and antibiotics has decreased the need for antitoxins administered in various serums. This change in therapy has materially reduced the incidence of serum disease but has increased the amount of drug allergy. One of the most widely used antibiotics is penicillin, and the medical literature contains many reports of allergic reactions to it. Waldbott[8] was the first to report an anaphylactic death from penicillin. Fortunately the number of deaths as well as the near fatal cases such as the one reported by Irwin, et al.[9] have been small in number. Cortisone and ACTH offer little in these severe anaphylactic reactions, which run their course too quickly for these hormones to be effective. The common manifestations of penicillin sensitivity are urticaria and angioneurotic edema for which cortisone and corticotropin are seldom indicated unless symptoms occur in unusually prolonged or severe form. Here several short courses of cortisone or corticotropin have been used successfully in alleviating symptoms.

In the field of drug allergy repeated emphasis must be placed on the necessity for careful consideration of the need for such medication and the history of previous use of the agent. Without question penicillin and other antibiotics have been most useful in the field of bacterial disease, but penicillin has been prescribed often for conditions in which no bacteriologic indication existed. Many people have been subjected, therefore, to possible sensitization for no good reason.

Discussion

Cortisone and corticotropin do not appear to destroy antibodies. Initial observations suggest that cortisone causes red blood cells to form in vivo aggregates. Whether this phenomenon has anything to do with immunologic processes remains to be determined. Bloch and Powell[10] studied aggregates of red cells found in the blood of patients with various bacterial diseases with an electron microscope. The red cells in these aggregates had altered surfaces. An irregular, amorphous coating covered the entire surface, and bridges between cells were found. Ebert and Wissler[11] observed red cell aggregates forming in blood vessels in tissues of a rabbit's ear chamber during anaphylaxis. These aggregates were seen to clear when cortisone was used. Further work must establish or deny the presence of these aggregates in allergic disease and must determine the ability of cortisone to destroy or enhance these aggregates.

The main emphasis in the clinical approach to allergic disease should continue to be concentrated in the field of the detection and removal of offending antigens and in hyposensitization therapy when necessary. Prevention is the important principle in serum disease and in drug allergy. Cortisone and corticotropin, however, are most useful in selected cases of allergic disease.

Summary

1. Effects of corticotropin on the cellular and circulating antibodies of hay fever are discussed.

2. Reactions of these hormones on small blood vessels are considered.

3. The importance of certain basic principles of allergy is reaffirmed.

4. The use of cortisone and corticotropin in selected cases of asthma, serum sickness and drug allergy is discussed.

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Editorials

Postgraduate Medicine

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THE PATIENT WHO CONTROLS DIABETES

THE individual who escapes smallpox, diphtheria and typhoid deserves no credit, because his good fortune is largely due to governmental health regulations. This does not hold for diabetes, because freedom from it in those hereditarily predisposed depends to some extent on the individual's avoidance of that contributory factor—overweight. The control of diabetes is dependent on a rigid regimen of diet, exercise and insulin—morning, noon and night—all the length of one's days.

Half a century ago it was recognized that the exceptionally wise diabetic in middle life often lived long, and that a few such persons survived even longer with their diabetes than their contemporaries of similar age without it. To such, a bronze medal was awarded by the New England Deaconess Hospital as long ago as 1930. The bronze medal was replaced by a silver medal if the fortunate recipient increased the duration of his life to half again that expected and, exceptionally, a gold medal was given when the duration of the life expectancy was doubled. At the beginning, the responsible factors in attaining a bronze medal were chiefly the patient's common sense and will power in resisting carbohydrates. When insulin arrived, lengthening the life of the average diabetic from 4.9 to 15 years and raising the average age at death from 44 to 64 years, the granting of a medal for exceeding one's life expectancy became almost commonplace, because so many deserved it.

Then gradually the thought developed that Health as well as Life should be recognized, because although so many patients lived long, at the same time many were distressingly handicapped by serious diabetic complications in the eyes, kidneys and arteries. Thereupon, in 1948, the Advisory Committee of the Diabetic Fund of the Boston Safe Deposit and Trust Company, with the artistic help again of Amelia Peabody, created the Quarter Century Victory Medal which could be awarded to those who not only lived a quarter century with diabetes but also were sound in health as certified by a physical examination, which included an expert opinion of an ophthalmologist and of a radiologist.

The purpose of this Quarter Century Victory Medal was threefold: (1) It recognized the moral fiber of the patient in addition to his knowledge and use of diet, exercise and insulin, and his trust in a scientific attack upon the disease; (2) it encouraged other diabetic patients above all by the example of these individuals who had lived so long and were so healthy, and (3) the Advisory Committee felt that if the life stories of such exceptional patients were analyzed, hints for the better treatment of even millions of other diabetics could be assembled. Up to now, 46 such medals have been granted.

An outstanding and cheerful feature of

these patients is that they are asymptomatic—no complaints. What a contrast to the usual diabetic, even after 10 years of the disease! As a matter of fact, since the inauguration of this series not one patient has died, so that in 1953 the average duration of their diabetes is 30 years. Women predominate, 28 to 18. The average age at onset of diabetes is 14.7 years, the range being 2 to 32 years with only 2 patients 30 years of age or older at onset. Of the women, 20 have married and so far have 19 children, and of the men, 15 have married and have 35 children; one of the men now has six children ranging in age from 5½ to 19 years, the youngest having been born 23 years after the onset of his father's diabetes. Heredity is known to be a positive factor thus far in 25 of 42 cases or 60 per cent. Only 54 children from 35 marriages have been born, or 1.5 children per marriage, thus showing that the opportunity for propagation of diabetes is not very great. This is in striking contrast to a recent survey by Dr. Priscilla White who permits me to state that among a hundred children ranging up to 18 years, of 75 diabetic mothers, she found 6 definite diabetics and 5 others chemically diabetic, in addition to 15 who were on the borderline. Among fathers the figures are less striking.

Searching for light on treatment, it is evident that these patients, particularly the younger ones, went through a Spartan regimen during the first few years they had the disease. Only gradually, after the early period, were their diets increased in carbohydrates and calories, and even if later they became less rigorous, only temporarily did their diets become liberal by modern standards, despite the use of insulin. The diet at present is not known. The dosage of insulin averaged 47 units for 41 cases, the range being 16 to 100 units with 3 patients taking between 80 and 89 units, and 15 from 30 to 40 units.

The number of persons who could acquire the Quarter Century Victory Medal should increase by leaps and bounds, particularly because of our better knowledge of diet and the value of exercise and insulin. It is desirable that the number should increase, because each Medal Case is a striking example to other diabetics. Each case creates a needed standard. Doctors universally should have their own Medal Cases for their own encouragement. Changes in criteria for reaching the decision as to whether an individual deserves a medal are desirable. It is pathetic to withhold recognition from a patient in whose artery of the ankle there is only a tiny fleck of calcium, because such lesions are so common at middle life in nondiabetics. Perhaps special rules for awards can be devised for diabetics who acquire the disease at the age of 40 years and above.

ELLIOTT P. JOSLIN

HOSPITAL INSURANCE

At this time about 80 million people—one-half the population—are covered by insurance against the costs of hospitalization. This is the major source of hospital income. The remaining noninsured people, the indigent, the low-pay worker, must be cared for by the use of community funds. Philanthropic contributions are steadily decreasing. "The total average expense per patient day in nonprofit general term hospitals in 1951 was $18.01 and the income from patients only $16.55."

The amounts contributed by 25 municipal community chests in 1935 was 16.5 per cent of total hospital income; in 1950, it was 4.9 per cent.

In the United States, out of a total civilian population of 159,000,000, 41 per cent or 63,600,000 are gainfully employed. With their dependents they make up 138,000,000 people. The unemployed labor force with their dependents make 3,141,000. Authorities estimate that the entire labor force can be covered by voluntary hospital prepayment plans by 1957 to 1962.

Among those listed as not possible to bring under voluntary plans are the aged, the indigent, the handicapped, the unemployed, and the marginally indigent who earn only a bare subsistence. There are 13.2 million over 65 years of age, of whom less than one-fourth are employed. Old people have more disabil-

ity and are disabled longer than young people. About one-half the old people receive some benefits from security plans. These sums in more than one-half the cases are under $2000 per year.

Estimates indicate the cost of hospital care for the unemployed and their dependents would reach $100,000,000 annually. Unemployment compensation reaches less than one-fourth the annual weekly budget of the city worker.

The problem of Blue Cross plans today is the battle of the benefits. The plans which provide the most benefits attract the most people, notwithstanding increased costs. Benefits mean number of days covered and such auxiliary services as drugs, laboratory, x-ray, anesthesia, oxygen, blood, radium, maternity care, on to tuberculosis, mental disease, drug addiction and communicable diseases. Frankly the patient does not want to be surprised by an unexpected bill for auxiliary services two or three times as big as his hospital bill. And doctors do not want to be considered as auxiliary services and depreciated into the status of technicians. And technicians have been standardized at such high levels that they are getting as expensive as—maybe even more expensive than—specialists.

MORRIS FISHBEIN

MEDICAL EDUCATION IN MISSISSIPPI

MISSISSIPPI is a rural state with 70 per cent of its people living in rural areas. At the end of the war, the number of physicians in the state was found to have decreased each year since 1909 from a high of 2,054 to a low in 1946 of 1,112. In the meantime the population had increased from 1,790,000 to 2,186,000. The actual number of doctors practicing in 1946 was only 915 and the number of persons per physician had increased from 871 in 1909 to 1,966 in 1946.

In 1946 the legislature passed laws which created the Mississippi State Medical Education Board, a Commission on Hospital Care to plan the construction of hospitals and health centers, and it provided for the construction of a 4-year medical school at Jackson. Nursing needs were to be studied and met and a Commission on Hospital Care was also to establish a statewide program of voluntary hospitalization insurance.

The fundamental recommendation of the State Medical Education Board was the provision of loans to students who guaranteed by contract to return to the state of Mississippi after graduation and one-year internship to engage in the practice of medicine in a rural area. If the student elected to remain in the approved area for 5 years, the entire loan, plus interest, was cancelled at the rate of one-fifth per year. He might, however, elect to repay the balance of his loan with interest at the end of 2 years. Since the object of the program is to increase the supply of general practitioners, arrangements are not made for residencies in specialties. Three of the scholarship recipients died before completion of their contract and the possibility of health examinations for applicants is being considered.

Dr. Felix J. Underwood, who has been executive officer of the Mississippi State Board of Health since 1924, has now rendered a report[1] of progress. The supply of physicians in the state is on the increase and has risen from 1,112 in 1946 to 1500 in 1953. The 4-year medical school is under construction in Jackson and will accommodate 400 medical students and 100 nursing students; a teaching hospital of 350 beds is also under construction. Thirty-eight new hospitals have been constructed and equipped and 5 more are under construction. Actually 2,250 hospital beds have been added and 895 more beds are under construction.

A statewide program of voluntary hospitalization and surgical insurance was established in 1948 and now has a membership of 250,000. Appreciation is given to the federal funds for hospital construction provided under the Hill-Burton Act. In addition, state, local and private funds have been reached. All the costs of the medical education scholarship loan program, the nursing education program, the hospital and surgical insurance program and the 4-year medical school project and more than

one-half of all hospital and health department construction costs have been paid with state, local and private funds.

The example of Mississippi thus stated without ornamentation or literary effusion is in itself an indication of what can be accomplished with proper leadership and an acceptance of the basic principle of American voluntary efforts.

MORRIS FISHBEIN

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MEDICAL HISTORY OF WORLD WAR II

Shortly after the end of World War II, a committee was organized under the auspices of the Division of Medical Sciences of the National Research Council to aid the Surgeon General in developing a medical history of the second World War. Unfortunately the work never really got under way; the first book[1] dealing with a small fragment of the problems has just been published. No one knows when, if ever, any more will appear and the portents do not seem exceedingly favorable.

In the meantime in Great Britain the first volume of the medical history of the second World War entitled "The Army Medical Services: Administration" has just appeared, with the authorship credited to Dr. F. A. E. Crew who is professor of public health in the University of Edinburgh. In its issue for June 13, 1953, the London *Lancet* has a forthright review of this first volume of the British medical history of the second World War. The review criticizes, of course, not only the book but also the services that it reflects. To quote, "The uncertainty in planning the medical services of the nation for war makes a sorry story. The pull-devil-pull-baker between the Armed Forces and the Ministry of Health took place across the Cabinet table. The first knew the number of doctors needed for the fighting Forces in being and projected, and perhaps they overestimated their needs. The second had been warned of astronomical casualties from aerial attack at home and believed that they could not spare a man. Perhaps not so much harm would have been done if the fight had been settled 12 months earlier, irrespective of the issue. . . . All this is described critically and without acrimony, but it is past history."

This quotation would seem to be just as applicable to what went on here in the United States. Unfortunately we have not had the volume discussing administration, organization, personnel or any of these fundamental matters; therefore, we can only say that perhaps we will have to take our medical history of the second World War secondhand from Great Britain. The final paragraph of the review in the London *Lancet* is almost equally applicable to what goes on here in the United States. It reads, "Is there any other country which would entrust an official military history to a distinguished geneticist who now holds a chair of public health? To quote the preface, 'the author alone is responsible for . . . the opinions expressed.' They are shrewd and they aim straight, but they are fair and, as far as we may judge, they will be generally accepted. As an enlightened presentation of fact the book is a masterpiece." Who is really going to produce the official American medical history of the second World War? In my own mind I have considerable doubt as to whether it will ever be produced.

MORRIS FISHBEIN

1. The Physiologic Effects of Wounds. By the Board for the Study of the Severely Wounded, North African-Mediterranean Theater of Operations, Medical Department, United States Army, Surgery in World War II. Office of the Surgeon General, Department of the Army, Washington, D.C., 1952.

KOPLIK'S SPOTS IN MEASLES

In 1896, Henry Koplik of New York described in the *Archives of Pediatrics* the presence of spots on the mucous membrane of the mouth in the early stages of measles which have become known throughout the world as Koplik's spots. In 1898, he published a second paper citing 16 cases in which the disease was diagnosed merely by this sign and a final paper was published in the *Medi-*

cal News in 1899. Since that time, attention has been called to the fact that other observers had noticed these spots before Koplik. In 1873, Monti of Vienna mentioned such spots noticed 12 to 24 hours before the appearance of the eruption of measles. Then in 1895 Filatow of Russia drew attention to delicate whitish tags of mucous membranes which he had observed before the appearance of the rash. However, W. R. Bett, eminent British medical historian, calls attention to the fact that none of these descriptions compares with Koplik's classic account in fullness, accuracy or tone of conviction.

Now comes a new report from Wurzburg, Germany, that one Fr. Rinecker of Wurzburg, during an epidemic of measles in the winter of 1853-1854, observed whitish spots on the lips, gums and sometimes on the tip of the tongue in measles. Microscopically leukocytes and mucus were found as in stomatitis. This is urged by Dr. J. Ströder of the Children's Clinic in Wurzburg as actually the first observation published about the spots now named after Koplik.

Dr. Ludvig Hektoen called attention to a report by a Dutch physician whose observation also antedated that of Koplik. However, none of this should detract from the quality of Koplik's study or his report. In making his record Koplik searched the available textbooks and periodical references. His description is lucid. He extended his studies and repeated them and he persisted until their significance was accepted.

MORRIS FISHBEIN

WHAT IS A PATHOLOGIST?

ACCORDING to the dictionaries a pathologist is one learned or skilled in pathology and pathology is "that branch of medicine which treats of the essential nature of disease, especially of the structural and functional changes which are caused by disease." The new Thorndike-Barnhart, which is a popular dictionary, now defines the use of the word pathology not only for the study of the causes and nature of disease but also for "unhealthy conditions or processes caused by a disease." This is a definition brought about by inaccurate usage of the term which has apparently become so popular now as to be acceptable.

One of the most clever columns published in any medical journal is the one called "In England Now" which appears regularly in the London *Lancet* and which is a running commentary on medicine by peripatetic correspondents. It is almost invariably worth reading and occasionally comes up with a gem. Such is the item which begins by saying that a pathologist, according to the use of the word in Edinburgh, is "a thoroughbred morbid anatomist and histologist." Then comes a brief description of a pathologist and of his work which deserves to be enshrined among the medical classics. It follows:

"The pathologist's apprenticeship is long and hard. You are blooded in the deadhouse, whence you graduate to biopsies, and if you manage to avoid pricking your finger, you become, when bald or greying, an authority. As such, your function is to pronounce upon the difficult section. The difficult section may originate anywhere in the region; born in obscurity, it travels by devious routes, pausing here and there at conferences and laboratory meetings, and finally comes to rest on your bench when you are out for lunch. It always consists of innumerable small round cells of a nondescript type, and though recognisable tissues, varying from case to case, may be present, the Thing Itself is as clueless and inscrutable as the Sphinx. Pictures of it are common in the journals, where it is variously described as sarcoma, carcinoma, blastoma, reticulosis, hyperplasia, a peculiar inflammatory reaction, or an atypical this or that. If you send it to a panel of experts, they will suggest all these possibilities, though perhaps in a different order. The correct diagnosis is of course *incognoma* or *incognitis* (whichever you prefer). In my report I explain this in simple language, and—as requested—enclose a modest bill, but I can't remember ever being paid for my candour."

MORRIS FISHBEIN

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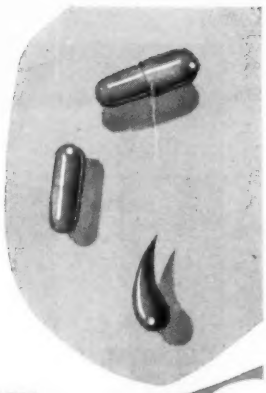

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2. Zelman, S.: Arch. Int. Med. *90*:141, 1952.

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THE MEDICAL Bookman

► CLINICAL ENDOCRINOLOGY

By Lewis M. Hurxthal, M.D. and Natalija Musulin, M.D. 2 volumes. 1,599 pages with 482 figures, 146 charts and 1 color plate. 1953, J. B. Lippincott Company, Philadelphia. $24.00.

A monumental work on endocrinology has come from the Department of Internal Medicine of the Lahey Clinic and the author has had the aid of a member of the staff of the Cooper Clinic in Camden, New Jersey. The work obviously is based on a tremendous clinical experience in a clinic which has been interested in endocrinology for many years. The great clientele of the Lahey Clinic has been thoroughly studied and the authors have developed references to periodical literature on a comprehensive scale. The bibliographies are extensive but nevertheless critically chosen, and the work may be said to be the most complete reference work in endocrinology thus far available.

The entire text is in outline form with historical references, physiology, diseases of the endocrine glands and of organs which have both endocrine and nonendocrine activities, and reference also to metabolism and treatment. A comprehensive index makes references to any phase of the subject simple and it enables any general practitioner or clinician to orient himself in the vast new field which is of such great significance because of the development of useful therapeutic preparations. Especially important to the clinician is the inclusion of numerous case reports in condensed form with preparation also of an outline which takes up family and past medical history, chief complaint, history of the present illness, physical examinations, laboratory data, roentgenographic observations, treatment, possible diagnoses and a complete record of progress followed by comment. This method of teaching is determined by experience as most useful.

Special importance attaches to the illustrations which were chosen for their ability to teach and which include particularly many charts showing the nature of the study given to the patient, the record of the case and comparison with other cases.

M. F.

► MORRIS' HUMAN ANATOMY
A Complete Systematic Treatise

By J. Parsons Schaeffer, M.D., The Jefferson Medical College, Philadelphia, Pennsylvania. Ed. 11. 1,718 pages with 1,220 figures. 1953, The Blakiston Company, New York. $16.00.

The eleventh edition of Morris' Anatomy has been brought up-to-date with some sections extensively rewritten and others revised. Its general appearance is more attractive in the combination of large type for the major portion of the text, with small type set in double columns for pertinent material which otherwise might have had to be omitted because of space.

Embryologic explanations are included at convenient places in each section as well as in the section on Developmental Anatomy; text references are made at appropriate locations in regard to clinical aspects and relations.

BNA terminology in Anglicized form has been continued, but spelling and compounding of words have been adapted to conform with present-day trends.

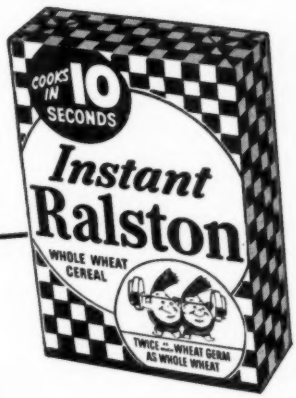
Many new illustrations have been added, a number of which are roentgenograms showing clinical aspects of the anatomy under discussion.

Each section has a revised bibliographic reference list alphabetized by authors which is easier to consult than the forbidding-looking listing in running order, as in the older editions.

I. P.

(Continued on page A-60)

Why



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► OFFICE ORTHOPEDICS

By Lewis Cozen, M.D., Assistant Professor of Orthopedic Surgery, College of Medical Evangelists, Los Angeles. Ed. 2. 304 pages with 191 illustrations. 1953, Lea & Febiger, Philadelphia. $5.50.

Designed primarily to aid the busy practitioner who is in need of immediate reference is this second edition of "Office Orthopedics." Confining the subject matter to diagnosis and care of the ambulatory patient, the volume is a well organized, systematic presentation of the more common bone and joint problems encountered in an office or outpatient clinic.

It is not the intention of the author to include all possible methods of treatment for patients who need not be hospitalized. His plan, rather, is to present a routine of therapy that has been successful for him. The book is well balanced. No particular aspect receives undue consideration. The content is regarded by the author as that most frequently seen in general practice. He has completely covered this viewpoint. Technical considerations are entirely deleted except for short descriptions of minor procedures.

The book is easily read, with the drawings and accurate photographs well placed to aid in definition. Its unique value will find realization in the profound gratitude of those who endeavor to treat skeletal diseases.

H. O'P.

► THE MANAGEMENT OF ABDOMINAL OPERATIONS

Edited by Rodney Maingot, F.R.C.S. 1,253 pages with 328 figures. 1953, The Macmillan Company, New York. $24.00.

"The Management of Abdominal Operations," edited by Rodney Maingot and written by 33 foremost British physicians and surgeons, is a most comprehensive and complete coverage of the care of patients undergoing treatment for abdominal conditions.

The first 18 chapters, including 400 pages, deal with general considerations involved in abdominal operations. Conditions affecting the risk of such operations are discussed in detail, and the preoperative and postoperative care of the patient and the complications likely to be encountered after surgical intervention are likewise considered. Excellent chapters are included on blood transfusions, shock, and water and electrolyte balances. The physiologic aspects of these problems are included, as well as the therapeutic aspects.

The second part of the book, comprising 29 chapters and covering 800 pages, takes up the regional considerations of abdominal operations. Adequate discussions of lesions and surgical procedures on the esophagus, stomach, liver, pancreas and other abdominal viscera are presented. For the most part, a fair evaluation of controversial points is given. A chapter on the management of abdominal operations in children is included.

Part 3 of the book includes 2 chapters dealing with aseptic technics and clinicopathologic values in health and disease.

The book is printed on glossy paper stock and the print is easy to read. It fills a need in that it supplies complete information necessary in the management of abdominal operations and is much more thorough than the usual textbook of surgery.

O. H. B.

► THE 1952 YEAR BOOK OF ENDOCRINOLOGY

Edited by Gilbert S. Gordan, M.D., Assistant Professor of Medicine, University of California School of Medicine, San Francisco. 400 pages, illustrated. 1953, The Year Book Publishers, Chicago. $5.50.

Articles on endocrines culled from a great many journals received between January 1952 and January 1953 are included in this review which was ably edited by Dr. Gilbert S. Gordan.

This reader enjoyed the pithy—sometimes subtly humorous—editorial notes following many of the quotations from scientific papers. As an example there is the reference to "The Citadel," by A. J. Cronin, in a note following the discussion on myxedema insanity.

The adrenals occupy more pages in the book than any other individual endocrines—with the thyroid gland a close second. This is understandable in view of the many excellent articles in this field during the last few years.

Laboratory tests come in for considerable discussion, and the relative merits of the new and the old are brought out in a straightforward

(Continued on page A-62)

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1.0 cc. contains 194 mg. (3 grains) Quinidine Sulfate, USP, in a special stabilizing, painless inert solvent.

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QUINIDATE-MRT, Capsules-in-Oil—(3 grain)
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by normal appearance at birth with subsequent evidence of virilism and somatic pre-

which is probably the commonest clinical manifestation of excessive function of the ad-

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New preparations of Veratrum Viride*
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Available:

Verastan Tablets-MRT, 100 mg

Each tablet contains the total activity of Standardized Veratrum Viride, MRT-100 mg. (1 MRT Potency Unit)

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Each teaspoonful (5cc) contains the total activity of Standardized Veratrum Viride, MRT—

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Further information to physicians upon request

Ref:* Marvin R. Thompson and Robert E. Thompson:
Reported before the A.Ph.A. Convention, Scientific Section, Salt Lake City, Aug. 20, 1953.

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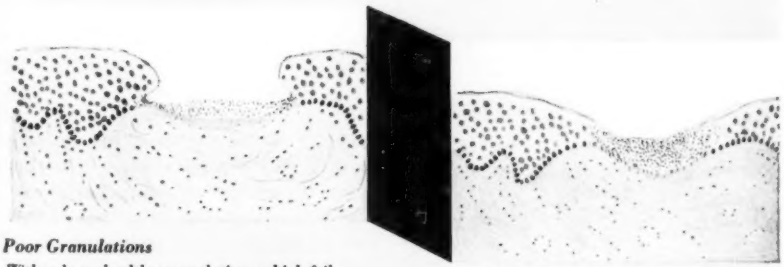
brand of water-soluble chlorophyll derivatives

ointment
solution (plain)

promotes the growth of healthy granulations



Poor Granulations
With pale, unhealthy granulations which fail to grow from depths of lesion, epithelium shows no tendency to cover defect.

Healthy Granulations
After healthy granulation tissue fills depths of lesion, epithelium will spread rapidly to cover surface of defect.

"Healthy granulations lead to normal healing." This dictum, recognized by every physician, delineates the special value of CHLORESIUM.

- "...Chloresium Ointment tended to produce a clean granulating wound."[1]
- "...prompt, clean healing with firm granulation."[2]
- "...effective agents in facilitating growth of granulation tissue and epithelization."[3]
- "...an active agent in restoring affected tissues to a state conducive to normal repair."[4]

CHLORESIUM OINTMENT—1-ounce and 4-ounce tubes.
CHLORESIUM SOLUTION (Plain)—2-ounce and 8-ounce bottles.

Literature containing comprehensive information on the uses of chlorophyll in medicine will be forwarded on request. Reprints of recent papers are also available.

(1) Moss, N. H.; Morrow, B. A.; Long, R. C., and Ravdin, I. S.: Effectiveness of Chloresium in Wound Healing and Deodorant Effects, J.A.M.A. *140*:1336 (Aug. 27) 1949. (2) Niemiro, B. J.: Delayed Healing in Pilonidal Cyst Wounds, Journal Lancet *71*:364, 1951. (3) Combes, F. C.; Zuckerman, R., and Kern, A. B.: Chlorophyll in Topical Therapy, New York State J. Med. *52*:1025, 1952. (4) Lowry, K. F.: Management of Resistant, Nonhealing Skin Lesions, Postgrad. Med. *11*:523, 1952.

company inc. Mount Vernon, New York

manner. When certain once valuable tests have reached the stage where they are now only of historical interest, we like to be so told by competent authority so that we may keep up with diagnostic trends.

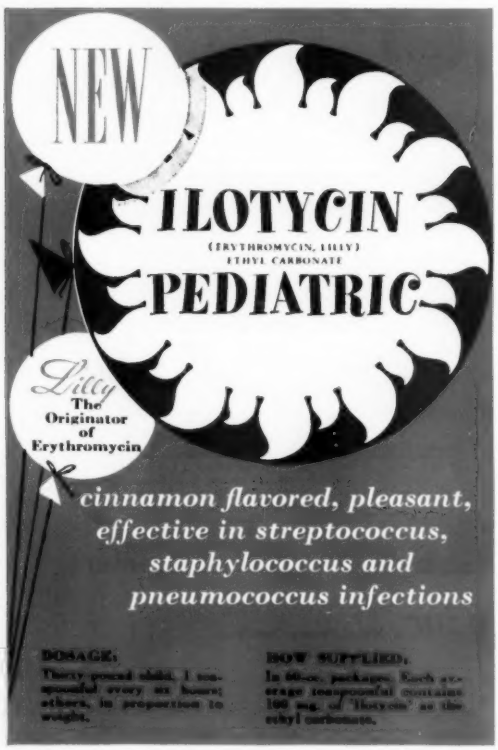
There are good separate subject and author indexes which add greatly to the usefulness of the volume.

R. F. E.

► THE BIOCHEMISTRY OF GASTRIC ACID SECRETION

By Edward J. Conway, M.D., Professor of Biochemistry and Pharmacology, University College, Dublin, Ireland. 185 pages with 37 illustrations. 1952, Charles C Thomas, Springfield, Illinois. $6.50.

Gastric acid secretion from its cellular and biochemical origin to the rationale of urea therapy of peptic ulcer is covered in this book.



The author begins with a description of the histology of the gastric mucosa from the standpoint of acid secretion, and develops the reasons for concluding that this secretion is a function of the parietal cells of the stomach wall. A discussion of the present evidence on the mode of stimulation of parietal cells is followed by an explanation of the fact that the parietal cell secretion is isosmotic with blood, and by an explanation of the existing high primary acidities. In an interesting discussion on the general biologic secretion of hydrogen ions, the author shows that gastric mucosa is not unique in its ability to secrete hydrogen ions and that the mechanism of acid secretion by yeast is a closely related phenomenon. After indicating that an organic acid respiratory catalyst is probably the direct donor of hydrogen ions, Conway discusses the "Redox" and other theories of acid secretion, along with a thermodynamic development of the work done in such secretion. Consideration is also given to the gastric potentials and their relationship to hydrochloric acid secretion.

The secretion of acid by the gastric mucosa creates the need for hydrogen ion replacement to the parietal cells. It is shown that the enzyme carbonic anhydrase catalyzes such a restoration through the ionization of carbonic acid. Concurrently, the enzyme urease catalyzes the formation of ammonia from urea to protect the nonparietal cells from the high acid concentration present. Urea therapy has evolved from the theory that this latter mechanism is deficient in the peptic ulcer patient.

The administration of urea to peptic ulcer patients has certain theoretical advantages over the commonly used antacids; urea forms part of the biochemical mechanism which may be defective in peptic ulcer patients, and it acts as an antacid only after being physiologically converted to ammonia. Conway reports encouraging results with 79 patients with persistent dyspepsia refractory to accepted treatment who did not suffer from renal damage. Urea therapy seemed of special value in the treatment of gastrojejunal or anastomotic ulcers.

The book is well documented (308 references) and up-to-date. The reader should be well grounded in the field of gastric acid secretion and be conversant with physicochemical technics. Useful subject and author indexes are included in the text.

G. M. N.

(Continued on page A-64)

NEW DRUG!

in the management of
PEPTIC ULCER
and
GASTROINTESTINAL SPASM

Malcotran*

10 MG. TABLET

A potent anticholinergic and ganglionic blocking agent.[1,2]
Selective gastrointestinal therapy.[3]
Suppresses gastrointestinal hypermotility.[3]
Reduces gastric secretion.[3]
Side effects absent or minimal.[3]
Convenient and economical q.i.d. dosage.

Supplied: **Uncoated, scored tablets of 10 mg., bottles of 100, 500, and 1000.**

* *'MALCOTRAN' is the Maltbie trade mark for New Drug dosage of homatropine methylbromide.*

1. Cahen, R. L., and Tvede, K.: Proc. Soc. Biol. & Med., 78:708, 1951.
2. Cahen, R. L., and Tvede, K.: J. Pharm. & Exp. Therap., 105:166, 1952.
3. Machella, T. E.: 1952-1953 (To be published).

MALTBIE LABORATORIES, INC. • NEWARK 1, N. J.

► A MANUAL OF CLINICAL ALLERGY

By John M. Sheldon, M.D., Professor of Internal Medicine; Robert G. Lovell, M.D., Instructor in Internal Medicine, and Kenneth P. Mathews, M.D., Assistant Professor of Internal Medicine, University of Michigan Medical School. 413 pages with 27 figures. 1953, W. B. Saunders Company, Philadelphia & London. $8.50.

This is an attractive book which is better than many others if only because a number of specialists contributed to the writing of it. There is a beautiful section on the various pollens. The section on food allergy will interest gastroenterologists. In some ways this section could be improved, but it is better than many others that the reviewer has seen. There is a section on allergy and headache. On page 230 cafergot is spelled wrong and the dosage should be 2 tablets to begin with and not 1. There aren't many persons who will respond well enough to the taking of 1 tablet.

There is a very good section in which the reader is told where, in the home or the office, he may run into the particular allergen that bothers him. For instance there are good lists of the allergens that will bother a carpenter, a painter, a baker or a photographer.

W. C. A.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

Twenty-Five Years of Sex Research; History of the National Research Council Committee for Research in Problems of Sex, 1922-1947. By Sophie D. Aberle, Member, National Science Board of the National Science Foundation, and George W. Corner, Carnegie Institution of Washington. 248 pages. 1953, W. B. Saunders Company, Philadelphia & London. $4.00.

Pituitary Chromophobe Adenomas; A Clinical Study of the Sellar Syndrome. By John I. Nurnberger, M.D., Research Associate, The Institute of Living, and Assistant Clinical Professor of Medicine (Neurology), Yale University School of Medicine, and Saul R. Korey, M.D., Associate Professor of Neurology, The School of Medicine, Western Reserve University. 282 pages, illustrated. 1953, Springer Publishing Company, Inc., New York. $7.00.

Cornell Conferences on Therapy. Editor: Harry Gold, M.D. Editorial Board: David P. Barr, M.D., McKeen Cattell, M.D., Frank C. Ferguson, Jr., M.D., Frank Glenn, M.D. and George Reader, M.D. Vol. 6. 287 pages. 1953, The Macmillan Company, New York. $4.00.

Dermatologic Formulary. From the New York Skin and Cancer Unit, Service of Dermatology, Dr. Marion B. Sulzberger, Director. Edited by Frances Pascher, M.D. 150 pages. Revised edition. 1953, Paul B. Hoeber, Inc., New York. $3.00.

The Gold-Headed Cane. (By William Macmichael, M.D.) A new edition with a foreword by James J. Waring, M.D. and a preface by William J. Kerr, M.D. Containing the text and illustrations of the fifth edition, including the introduction by George C. Peachey and his annotations. 186 pages, illustrated. 1953, Charles C Thomas, Springfield, Illinois. $6.50.

Nervous Transmission. By Ichiji Tasaki, M.D., Central Institute for the Deaf, St. Louis, Missouri. 164 pages, 138 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $7.50.

Therapeutics in Internal Medicine. Edited by Franklin A. Kyser, M.D., Assistant Professor of Medicine, Northwestern University Medical School, Chicago. Ed. 2. 830 pages. 1953, Paul B. Hoeber, Inc., New York. $15.00.

Autonomic Nervous System. By Albert Kuntz, M.D., Professor of Anatomy, St. Louis University School of Medicine. Ed. 4. 605 pages with 94 illustrations. 1953, Lea & Febiger, Philadelphia. $10.00.

Surgical Forum. Proceedings of the Forum Sessions, Thirty-Eighth Clinical Congress, American College of Surgeons, New York City, September 1952. Surgical Forum Committee: Owen H. Wangensteen, M.D., J. Garrott Allen, M.D., Warren H. Cole, M.D., Robert E. Gross, M.D., Carl A. Moyer, M.D., I. S. Ravdin, M.D., H. B. Shumacker, M.D. 716 pages, illustrated. 1953, W. B. Saunders Company, Philadelphia & London. $10.00.

The Diabetic Neuropathies. By Joseph I. Goodman, M.D., Siegfried Baumoel, M.D., Leonard Frankel, M.D., Louis J. Marcus, M.D. and Sigmund Wassermann, M.D., Mount Sinai Hospital, Cleveland, Ohio. Edited by Willard O. Thompson, M.D., University of Illinois College of Medicine, Chicago. 138 pages. 1953, Charles C Thomas, Springfield, Illinois. $4.75.

The Surgery of Infancy and Childhood; Its Principles and Techniques. By Robert E. Gross, M.D., William E. Ladd Professor of Children's Surgery, The Harvard Medical School, Boston. 1000 pages with 1,488 illustrations on 567 figures. 1953, W. B. Saunders Company, Philadelphia & London. $16.00.

Man's Back. By Theodore A. Willis, M.D., Formerly Head, Department of Orthopedic Surgery, St. Luke's Hospital, Cleveland. 161 pages with 210 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $9.50.

Surgery of the Pancreas. By Richard B. Cattell, M.D. and Kenneth W. Warren, M.D., The Lahey Clinic, Boston. 374 pages with 100 figures. 1953, W. B. Saunders Company, Philadelphia & London. $10.00.

Sectional Radiography of the Chest. By Irving J. Kane, M.D., Consultant in Chest Diseases, United States Naval Hospital, St. Albans, New York, with a foreword by Edward D. Churchill, M.D. 154 pages with 101 figures. 1953, Springer Publishing Company, Inc., New York. $7.50.

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ACTIONS AND USES: PENTRESAMIDE Tablets provide the combined antibacterial activity of penicillin and sulfonamides—in many susceptible infections more effective than either agent used alone. They are especially useful in mixed infections.

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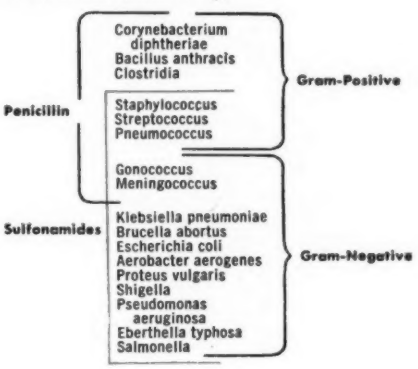
DOSAGE: Adults, 1 or 2 tablets or teaspoonfuls q.i.d. Children, by weight and condition. Dosage schedule on request.

Wider Antibacterial Range



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for more blood flow . . . Priscoline

hydrochloride
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orally and parenterally effective

Average rise in skin temperature of toes in 15 patients after a single intravenous injection of Priscoline. (Reedy, W. J.: J. Lab. & Clin. Med. 37:365, 1951.)

Of the peripheral vasodilating agents available "Priscoline, given orally in doses of 0.025 to 0.050 Gm. every three or four hours, appears to be the most practicable for prolonged clinical trial." (Cecil and Loeb: Textbook of Medicine, ed. 8, 1951, p. 1189.)

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